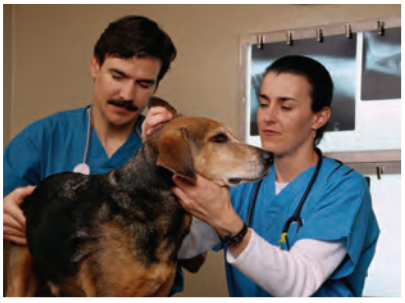

Missouri Veterinary Emergency Awareness Manual

Introduction

The Missouri Veterinary Medical Association (MVMA), Missouri Department of Agriculture (MDA), and Missouri Department of Health and Senior Services (DHSS) are working collaboratively to develop the Missouri Veterinary Emergency Awareness Program. This is a training and information-sharing program for veterinarians that will allow them to respond to outbreaks of animal disease that might originate through natural means or by an act of bioterrorism. The program utilizes multiple methods of communication, including videoconferencing to regional sites across the state, personal presentations at MVMA district meetings, newsletter articles, direct mailings to veterinarians, and material made available on the World Wide Web.

The impetus for this training is the growing threat to animal and human health presented by emerging/re-emerging infectious diseases as well as by the threat of a bioterrorist act. The risk of disease introduction into populations of companion animals, livestock, and poultry has increased dramatically as the global movement of animals and people has accelerated. The impact of the introduction of disease into these populations could be catastrophic. For example, the occurrence of foot-and-mouth disease in the United States would have enormous economic ramifications and its effect on the cattle industry would involve a long period of recovery. Even if a foreign animal disease that might be introduced into our country could be eradicated, it would most likely be at a very high cost. The outbreak of exotic Newcastle disease in Southern California in 2003 was successfully controlled, but only because of early detection and extremely intensive investigation and follow-up.

It is estimated that 75 percent of the emerging/re-emerging pathogens are zoonotic. Therefore, the public health impact of these diseases must always be considered. In some instances, sick animals may serve as a source of infection for humans. At other times, both animals and humans might fall ill from a common environmental exposure. The detection of illness in animals may be used as a “sentinel” event, presenting a warning of possible impending human cases that could be prevented or minimized through implementation of effective intervention measures. This situation would have the highest likelihood of occurring in an urban area in which there are higher concentrations of people, companion animals, and veterinarians.

In addition to the spread of disease by natural mechanisms, the possibility of introduction of infectious disease by terrorist activity must also be considered. This problem is compounded by the fact that many potential agents of bioterrorism (e.g., anthrax, tularemia, plague) also occur naturally. This necessitates the rapid reporting and investigation of these cases (in animals and humans), so that naturally occurring cases can be differentiated from those caused by an act of bioterrorism. Since almost 80 percent of the Category A and B bioterrorist agents are zoonotic, investigations of animal and human cases of these diseases will often be closely linked to each other.

The purpose of this manual is to provide veterinarians with condensed reference material regarding the major high consequence livestock pathogens and potential agents of bioterrorism. It is not intended to be comprehensive either in the number of diseases included in the manual or in its treatment of individual diseases. The manual consists primarily of fact sheets derived from the Iowa State University Center for Food Security and Public Health (CFSPH), which is a Centers for Disease Control and Prevention (CDC) Center for Public Health Preparedness. The CFSPH is CDC’s only Center for Public Health Preparedness that focuses on veterinary medicine and zoonotic diseases.

Additional materials in the manual include:

- Listing of individuals and agencies at the state and federal levels, along with contact information, who should be contacted in the event of an animal and/or public health emergency.
- Emergency response protocol for reporting foreign animal diseases.
- Listing of reportable diseases.
- Summary of general signs of reportable diseases in animals and poultry.
- Recommendations regarding biosecurity measures, methods for protecting livestock operations, and use of disinfectants.
- Reference chart to distinguish exotic Newcastle disease from highly pathogenic avian influenza.
- Reference chart to distinguish various vesicular diseases.
- Photographs to help in the diagnosis and differentiation of various infectious diseases, particularly vesicular diseases.

Recommendations and comments pertaining to the content of this manual may be addressed to representatives from the MVMA, MDA, and DHSS. Telephone numbers for these individuals are given in the emergency contact listing included with this manual.

The use of trade names in this manual is for the information of the reader. Such use does not constitute an official endorsement or approval by the MVMA, MDA, or DHSS.

Acknowledgement

Photographs of animal diseases in this manual are provided by the United States Animal Health Association, 1610 Forest Avenue, Richmond, Virginia 23288. The participation of the USAHA is gratefully acknowledged. Other information on foreign animal and zoonotic diseases is available on the web at *www.usaha.org*.

The MVMA, MDA, and DHSS extend their thanks to Dr. Michael Pfander, Cottage Veterinary Hospital, Springfield, Missouri for his help in preparation of this manual and his participation in the Missouri Veterinary Emergency Awareness Program.

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www.dhss.mo.gov
To report a public health emergency, call 1-800-392-0272.
This toll-free number is staffed 24 hours a day, seven days a week.

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Alternate forms of this publication for persons with disabilities may be obtained by contacting 1-866-628-9891.
Hearing and speech impaired citizens telephone 1-800-735-2966.

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TABLE OF CONTENTS

*The classification system chosen for this manual consists of the primary Category A and Category B bioterrorist agents (Section I), as listed by the Centers for Disease Control and Prevention, plus additional high-consequence livestock pathogens (Section II). These listings are not mutually exclusive, as some "high-consequence livestock pathogens" could be classified as "potential bioterrorist agents" and vice versa.

Section 1

Disease From Potential Bioterrorist Agents

Anthrax

Woolsorters' Disease, Cumberland Disease, Maladi Charbon, Malignant Pustule, Malignant Carbuncle, Milzbrand, Splenic Fever

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Etiology

Anthrax results from infection by *Bacillus anthracis*, a spore forming, Gram positive aerobic rod (family Bacillaceae).

Geographic Distribution

Anthrax can be found worldwide; it is particularly common in parts of Africa, Asia and the Middle East. In the United States, foci of infection occur in South Dakota, Nebraska, Mississippi, Arkansas, Texas, Louisiana and California, with smaller areas in other states.

Transmission

In animals, transmission is usually by ingestion. Herbivores usually become infected when they ingest spores on plants in pastures. Outbreaks typically occur in neutral or alkaline calcareous soil and are often associated with heavy rainfall, flood or drought; under optimal levels of moisture, temperature and other conditions, spores in the soil can revert to the vegetative form and grow to infectious levels. Contaminated bone meal and other feed can also spread this disease. Carnivores usually become infected after eating contaminated meat. Vultures and flies may spread anthrax after feeding on carcasses.

In infected animals, large numbers of bacteria are present in the hemorrhagic exudates from the mouth, nose and anus; when they are exposed to oxygen, these bacteria develop endospores and contaminate the soil. Sporulation requires oxygen and does not occur inside a closed carcass; opening an infected carcass for necropsy should be avoided. Anthrax spores can remain viable for decades in the soil or animal products such as dried or processed hides and wool. Spores can also survive for 2 years in water, 10 years in milk and up to 71 years on silk threads. Vegetative organisms are thought to be destroyed within a few days during the decomposition of unopened carcasses.

Humans usually develop the cutaneous form of anthrax after skin contact with infected animal tissues such as hides, wool, bone meal and blood. Biting flies that feed on infected animals or carcasses may also be able to transmit this form. Inhalation anthrax is seen after inhalation of spores from contaminated dust or animal products. Intestinal anthrax results from the ingestion of contaminated meat containing viable spores.

Anthrax has been studied as a weapon by the United States, Iraq, the former Soviet Union and probably other countries.

Disinfection

Anthrax spores are resistant to heat, sunlight, drying and many disinfectants. Spores can be killed with 2% glutaraldehyde formaldehyde or 5% formalin; soaking overnight is recommended. A 10 % NaOH or 5 % formaldehyde solution can be used for stockyards, pens and other equipment. Sterilization is also possible by heating to 121°C for at least 30 min. Blowtorches can be used to disinfect buildings.

Exposed arms and hands can be washed with soap and hot water then immersed for one minute in a disinfectant such as an organic iodine solution or 1 p.p.m. solution of mercuric perchloride. Clothing should be cleaned and boiled.

Infections in Humans

Incubation Period

The incubation period in humans is 1 to 7 days; typically, symptoms of inhalation anthrax appear after 2 to 5 days and symptoms of cutaneous anthrax after 2 to 3 days. After accidental aerosol release in the Soviet Union, cases continued to appear for up to 6 weeks.

Clinical Signs

Three forms of disease are seen in humans: cutaneous anthrax, intestinal anthrax and inhalation anthrax.

Cutaneous anthrax is characterized by a papular skin lesion, which becomes surrounded by a ring of fluid–filled vesicles. The central papule ulcerates, dries and develops a depressed, black scab. The skin lesion is usually painless, but is often surrounded by significant edema. Swelling on the face or neck may occlude the airways; lesions on the face or neck can also develop into meningitis. Fever, lymphadenopathy, pus and pain are seen only if secondary infections occur. Lesions often resolve spontaneously but disseminated, fatal infections occur in approximately 20%.

Intestinal anthrax develops after eating contaminated meat. The initial symptoms may be mild and can include malaise, a low fever and mild gastrointestinal symptoms. Severe symptoms then develop acutely and may include high fever, dyspnea, cyanosis, disorientation and other signs of septicemia. Intestinal anthrax rapidly progresses to shock, coma and death.

Inhalation anthrax occurs after inhaling spores in contaminated dust. Natural infections are mainly seen among workers who handle infected hides, wool and furs. The clinical signs develop gradually and are nonspecific. Symptoms may include fever, tiredness, and malaise; a nonproductive cough and mild chest pain may be present. The symptoms often improve for several hours to 3 days; this period of improvement ends with the acute onset of severe respiratory distress, diaphoresis, stridor and cyanosis, followed by fatal septicemia and shock within one to two days.

Communicability

Person to person transmission of anthrax is very rare and has been reported only in cases of cutaneous anthrax.

Diagnostic Tests

Anthrax is diagnosed by finding the characteristic organisms in clinical samples or by isolating *B. anthracis*. Blood, fluid samples from skin lesions, aspirates of lymph nodes or spleen, or cerebrospinal fluid (in cases of meningitis) are stained with polychrome methylene blue (M'Fadyean's stain). *B. anthracis* organisms are square–ended, blue–black bacilli surrounded by a pink capsule. Bacteria are not always found in blood cultures during septicemia.

B. anthracis colonies on blood agar are white or gray, at least 3 mm diameter, nonhemolytic, and have a dry, ground–glass appearance and sometimes tails. Capsules may be demonstrated in mucoid colonies from cultures grown on nutrient agar with 0.7 percent sodium bicarbonate, incubated overnight under CO_2. *B. anthracis* is also susceptible to specific bacteriophages and exhibits a characteristic 'string–of–pearls' formation when grown with penicillin. Antibiotic treatment of patients may prevent isolation of the organism.

Treatment and Vaccination

Natural strains of *B. anthracis* are usually susceptible to a variety of antibiotics; most but not all natural strains are susceptible to penicillin. Effective treatment depends on early recognition of the symptoms: treatment for cutaneous anthrax is usually effective but inhalation and intestinal forms are difficult to recognize and mortality rates are much higher. Inhalation and intestinal anthrax may be fatal once symptoms appear, in spite of treatment. Supportive therapy may be necessary. Vaccines are available for humans who have a high risk of infection.

Morbidity and Mortality

In most countries, cases of anthrax occur infrequently and sporadically, mainly as an occupational hazard among veterinarians, agricultural workers, and workers who process hides, hair, wool and bone products. The cutaneous form accounts for more than 95% of natural anthrax infections. The intestinal form is rare but can occur in outbreaks associated with contaminated meat. Natural cases of inhalation anthrax are rare; however, aerosolized biological weapons would be expected to produce a high percentage of this form.

Estimates of the case fatality rates of untreated cutaneous anthrax range from 5 to 25%, while treated cutaneous anthrax has a very low mortality rate. Untreated inhalation and intestinal infections are almost always fatal; these infections may also be recognized too late for effective treatment. The case fatality rate for the intestinal form is estimated to be from 25% to 75%; the case–fatality rate for inhalational anthrax probably approaches 90 to 100%.

Infections in Animals

Species Affected

Many species can develop anthrax but susceptibility varies: rats and chickens are relatively resistant to disease while goats, sheep, cattle and horses are more susceptible. Anthrax has been seen in pigs, mink, cats and dogs fed contaminated meat.

Incubation Period

The incubation period is 1 to 20 days; most infections become apparent after 3 to 7 days. In pigs, the incubation period is usually 1 to 2 weeks.

Clinical Signs

In ruminants, sudden death may be the only sign. Staggering, trembling and dyspnea may be seen in some animals, followed by rapid collapse, terminal convulsions and death. In the acute form, clinical signs are apparent for up to 2 days before death. Fever and excitement may be followed by depression, stupor, disorientation, muscle tremors, dyspnea, abortion, congested mucous membranes and bloody discharges from the nose, mouth and

anus. Chronic infections, characterized by subcutaneous edematous swellings, are also seen; the ventral neck, thorax and shoulders are most often involved. This swelling may be widespread.

In horses, common symptoms include fever, chills, anorexia, depression and severe colic with bloody diarrhea. Swellings may be seen in the neck, sternum, lower abdomen and external genitalia. Affected animals usually die within 1 to 3 days but some animals can survive up to a week.

Sudden death may also be seen in pigs. Many pigs have mild chronic infections characterized by localized swelling, fever and enlarged lymph nodes, with eventual recovery. Some animals develop progressive swelling of the throat, with dyspnea and difficulty swallowing; these animals may suffocate. Intestinal involvement, with anorexia, vomiting, diarrhea or constipation, is less common. Recovered, asymptomatic animals may have signs of localized infections in the tonsils and cervical lymph nodes at slaughter.

Clinically apparent anthrax in dogs, cats and wild carnivores resembles the disease in pigs.

Communicability

Yes. Large numbers of bacteria are present in the carcass and in bloody discharges from body openings. Tissues including skin and wool can contain spores, which remain viable for long periods of time.

Diagnostic Tests

A presumptive diagnosis is often made by examining blood or other tissues for the characteristic bacteria. Blood clots poorly in anthrax cases and sampling may be done post–mortem. In pigs, bacteremia is rare and a small piece of aseptically collected lymphatic tissue is often used. *Bacillus anthracis* is a large Gram positive rod that may occur singly, in pairs or in chains; endospores are not formed inside the body but may be found under certain culture conditions.

Bacterial culture may be used for diagnosis. *B. anthracis* colonies on blood agar are white or gray, at least 3 mm diameter, nonhemolytic, and have a dry, ground–glass appearance and sometimes tails. Capsules may be demonstrated in mucoid colonies from cultures grown on nutrient agar with 0.7 percent sodium bicarbonate, incubated overnight under CO_2. *B. anthracis* is also susceptible to specific bacteriophages and exhibits a characteristic ‘string–of–pearls’ formation when grown with penicillin.

Other diagnostic methods include polymerase chain reaction to detect bacterial nucleic acids, immunofluorescence for bacteria in blood or tissues, or a chromatographic assay to detect antigens in the blood. Mouse or guinea pig inoculation is rarely used. Immunoblotting (Western blotting) and enzyme–linked immunosorbent assays (ELISAs) are available; however, serology is rarely used for diagnosis.

Treatment and Vaccination

Antibiotics may be effective if treatment is started early. Vaccines are available for livestock.

Morbidity and Mortality

Clinical infections in ruminants and horses are usually fatal; pigs often recover. In carnivores, mortality is relatively low.

Post–Mortem Lesions

Rigor mortis is usually absent or incomplete and the carcass is typically bloated and decomposes rapidly. Dark, tarry blood may ooze from the body orifices. Edema may be noted, particularly around the throat and neck, in horses. Necropsies should generally be avoided, to prevent contamination of the surrounding area with spores.

If the carcass is opened, signs of septicemia will be evident. The blood is dark, thick and does not clot readily. Edematous, blood–tinged effusions may be seen in the subcutaneous tissues, between skeletal muscles and under the serosa of organs. Hemorrhages, petechia and ecchymoses are often noted in the lymph nodes, abdomen and thorax; hemorrhages and ulcers are also common in the intestinal mucosa. Peritonitis and excessive peritoneal fluid may be seen. The spleen is usually enlarged and has a ‘blackberry jam’ consistency. The lymph nodes, liver and kidneys may be swollen and congested.

Pigs with chronic anthrax usually have lesions only in the pharyngeal area. The tonsils and cervical lymph nodes are typically enlarged and a mottled salmon to brick–red color on cut surface. The tonsils may be covered by diphtheritic membranes or ulcers. The surrounding area is usually edematous and gelatinous. Some pigs may have a chronic intestinal form, with inflammation and lesions in the mesenteric lymph nodes.

Internet Resources

Animal Health Australia.
The National Animal Health Information System (NAHIS)
http://www.brs.gov.au/usr–bin/aphb/ahsq?dislist=alpha

Centers for Disease Control and Prevention (CDC)
http://www.cdc.gov/ncidod/dbmd/diseaseinfo/anthrax_t.htm

FAO Manual on meat inspection for developing countries
http://www.fao.org/docrep/003/t0756e/t0756e00.htm

Material Safety Data Sheets–
Canadian Laboratory Center for Disease Control
http://www.hc–sc.gc.ca/pphb–dgspsp/msds–ftss/index.html#menu

Medical Microbiology
http://www.gsbs.utmb.edu/microbook

The Merck Manual
http://www.merck.com/pubs/mmanual/

The Merck Veterinary Manual
http://www.merckvetmanual.com/mvm/index.jsp

USAMRIID's Medical Management of Biological Casualties Handbook
http://www.vnh.org/BIOCASU/toc.html

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Botulism

Lamziekte, Shaker Foal Syndrome, Loin Disease, Limberneck, Western Duck Sickness, Bulbar Paralysis

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Etiology

Botulism is caused by botulinum toxin, a potent neurotoxin produced by *Clostridium botulinum* and a few strains of *C. baratii* and *C. butyricum*. *Clostridium botulinum* is an anaerobic, Gram–positive, spore–forming rod.

Botulism can result from the ingestion of preformed toxin or the growth of C. botulinum in anaerobic tissues. Seven types of botulinum toxin, designated A through G, have been identified. Types A, B, E and F cause illness in humans. Type C is the most common cause of botulism in animals. Type D is sometimes seen in cattle and dogs, and type B can occur in horses. Types A and E are found occasionally in mink and birds. Type G rarely causes disease, although a few cases have been seen in humans. All types of botulinum toxin produce the same disease; however, the toxin type is important if antiserum is used for treatment.

Geographic Distribution

C. botulinum is found worldwide and cases of botulism can be seen anywhere. In ruminants, botulism mainly occurs in areas where phosphorus or protein deficiencies are found. Botulism is seen regularly in cattle in South Africa and sheep in Australia. This disease is rare in ruminants in the United States, although a few cases have been reported in Texas and Montana.

Transmission

C. botulinum and its spores are widely distributed in soils, sediments in fresh and coastal waters, the intestinal tracts of fish and mammals, and the gills and viscera of shellfish. The bacteria can only grow under anaerobic conditions. Botulism occurs when animals ingest preformed toxins in food or C. botulinum spores germinate in anaerobic tissues and produce toxins as they grow.

Botulism in Humans

In humans, botulism is classified into three forms: foodborne, wound, and infant or intestinal botulism. Foodborne botulism is the most common form and occurs when humans ingest toxins in various foods. The foods associated with botulism are usually low acid (pH greater than 4.6) and may include home–canned foods, sausages, meat products, canned vegetables and seafood products. Commercial foods are occasionally implicated. Wound botulism occurs when an anaerobic wound is contaminated with C. botulinum, usually from the soil. Infant botulism is seen only in children less than a year of age. In this form, C. botulinum spores germinate in the intestinal tract and produce toxin. Honey has been associated with some cases of infant botulism but spores can also be found in many other sources. Adults with altered intestinal flora, secondary to gastrointestinal surgery or antibiotic therapy, may also be able to develop this form.

Botulism in Animals

Preformed toxins in a variety of sources, including decaying vegetable matter (grass, hay, grain, spoiled silage) and carcasses can cause botulism in animals. Carnivores, including mink and commercially raised foxes, usually ingest the toxins in contaminated meat such as chopped raw meat or fish. Cattle in phosphorus–deficient areas may chew bones and scraps of attached meat; a gram of dried flesh may have enough botulinum toxin to kill a cow. Similar cases occur in Australia, where protein–deficient sheep sometimes eat the carcasses of rabbits and other small animals. Ruminants may also be fed hay or silage contaminated by toxin–containing carcasses of birds or mammals. Horses usually ingest the toxin in contaminated forage. Birds can ingest the toxins in maggots that have fed on contaminated carcasses or in dead invertebrates from water with decaying vegetation. Cannibalism and contaminated feed can also result in cases in poultry.

The toxicoinfectious form of botulism corresponds to the wound and intestinal forms in humans. C. botulinum may grow in necrotic areas in the liver and GI tract, abscesses in the navel and lungs, or anaerobic wounds in the skin and muscles. This form of botulism appears to be responsible for shaker foal syndrome in horses. Toxi-

coinfectious botulism is also seen in chickens, when broilers are intensively reared on litter; the cause of this phenomenon is unknown.

Botulinum and Bioterrorism

In a bioterrorist attack, botulinum toxin could be delivered by aerosols, as well as food or water. After aerosol transmission, the clinical disease is expected to be similar to foodborne botulism.

Disinfection/ Inactivation

Botulinum toxins are large, easily denatured proteins. Toxins exposed to sunlight are inactivated within 1 to 3 hours. Botulinum can also be inactivated by 0.1% sodium hypochlorite, 0.1N NaOH, heating to 80°C for 30 minutes or 100°C for 10 minutes. Chlorine and other disinfectants can destroy the toxins in water.

The vegetative cells of *Clostridium botulinum* are susceptible to many disinfectants, including 1% sodium hypochlorite and 70% ethanol. The spores are resistant to environmental conditions but can be destroyed by moist heat (120°C for at least 15 min).

Infections in Humans

Incubation Period

The incubation period for foodborne infections is a few hours to 10 days; most cases become symptomatic after 18 to 36 hours. Wound infections may become evident within a few days to 2 weeks. The incubation period for intestinal or infant botulism is unknown. Inhalation botulism usually develops 12 to 36 hours after exposure, but in some cases the incubation period may be up to several days.

Clinical Signs

Foodborne Infections

In foodborne infections, gastrointestinal disturbances – including nausea, vomiting and abdominal pain – are often the first sign. Either diarrhea or constipation may occur. As the disease progresses, a symmetric, descending flaccid paralysis develops in the motor and autonomic nerves. The clinical signs may include blurred or double vision, photophobia, drooping eyelids, slurred speech, dysphagia, urine retention, a dry mouth and muscle weakness. In untreated progressive infections, descending paralysis of the respiratory muscles, arms and legs is seen. Fatal respiratory paralysis may occur within 24 hours in severe cases. Fever is not usually seen.

Wound Botulism

Wound botulism is very similar to foodborne infections; however, gastrointestinal signs are not usually present and patients may have a wound exudate or develop a fever.

Infant Botulism

Most cases of infant botulism occur in 2–week to 6–month–old babies. The first symptom is usually constipation. Other signs may include lethargy, weakness, excessively long sleep periods, diminished suck and gag reflexes and dysphagia with drooling. Some babies develop a weak or altered cry. In progressive cases, the infant may develop flaccid paralysis; a “floppy head” is typical. In severe cases, there may be respiratory arrest and death. The symptoms and severity of this disease vary considerably in different babies.

Intestinal botulism in adults

The initial symptoms of intestinal botulism in adults may include lassitude, weakness and vertigo. As the disease progresses, patients may experience double vision and have progressive difficulty speaking and swallowing. Other symptoms may include dyspnea, general muscle weakness, abdominal distention and constipation.

Communicability

No person–to–person transmission has been seen.

Diagnostic Tests

Botulism can tentatively diagnosed by the clinical signs and the exclusion of other neurologic diseases. The definitive diagnosis relies on identifying the toxin in feces, blood, vomitus, gastric aspirates, respiratory secretions or food samples. Feces are usually the most reliable clinical sample in foodborne or infant botulism; the toxin may be found for days or weeks in foodborne cases. Botulinum toxin is rarely found in the blood in adults but is occasionally detected in infants. The toxin can be identified by mouse inoculation studies (the mouse neutralization test), ELISAs or electrochemiluminescent (ECL) tests. Botulinum toxins can be typed with neutralization tests in mice. Serology is not useful for diagnosis, as small amounts of toxin are involved and survivors rarely develop antibodies.

C. botulinum can often be cultured from the feces in infant botulism or the wound in wound botulism. In foodborne cases, the food is usually cultured as well as tested for the toxin. C. botulinum is an anaerobic, Gram positive, spore–forming rod. On egg yolk medium, toxin–producing colonies usually display surface iridescence that extends beyond the colony. The iridescent zone around the colony is usually larger for C, D and E toxins.

Treatment and Vaccination

Supportive treatment, with respiratory support if necessary, is the cornerstone of treatment. Botulinum antitoxin, given early, may prevent the disease from progressing and decrease the duration of symptoms. In

foodborne illness, the amount of toxin in the gastrointestinal tract can be reduced with stomach lavage and enemas. Antibiotics and debridement are used in cases of wound botulism. Antibiotics are also used occasionally in foodborne cases, but are not generally recommended in infant botulism as they may change the intestinal flora. Investigational vaccines may be available for humans who have a high risk of exposure.

Morbidity and Mortality

Outbreaks of botulism can occur worldwide. Approximately 10 to 30 outbreaks are seen annually in the United States. In 1999, 107 cases of infant botulism, 26 cases of foodborne botulism and 41 cases of wound botulism were reported in the United States.

The death rate is high in untreated cases, but has been decreasing with improvements in supportive care. Before 1950, the mortality rate was 60%; currently, it is less than 5%. Recovery may be slow and can take several months or longer. In some cases, survivors report fatigue and shortness of breath for years.

Botulinum toxins are known to have been weaponized by several countries and terrorist groups.

Infections in Animals

Species Affected

Many species of mammals and birds, as well as some fish, can be affected by botulism. Clinical disease is seen most often in wildfowl, poultry, mink, cattle, sheep, horses and some species of fish. Dogs, cats and pigs are resistant; botulism is seen occasionally in dogs and pigs but has not been reported from cats.

Incubation Period

The incubation period can be 2 hours to 2 weeks; in most cases, the symptoms appear after 12 to 24 hours. Mink are often found dead within 24 hours of ingesting the toxin.

Clinical Signs

Botulism is characterized by progressive motor paralysis. Typical clinical signs may include muscle paralysis, difficulty chewing and swallowing, visual disturbances and generalized weakness. Death usually results from paralysis of the respiratory or cardiac muscles.

Ruminants

In cattle, the symptoms may include drooling, restlessness, incoordination, urine retention, dysphagia and sternal recumbency. Lateral recumbent animals are usually very close to death. In sheep, the symptoms may include drooling, a serous nasal discharge, stiffness and incoordination. Abdominal respiration may be observed and the tail may switch on the side. As the disease progresses, the limbs may become paralyzed and death may occur.

Horses

The clinical signs in horses are similar to cattle. The symptoms may include restlessness, knuckling, incoordination, paralysis of the tongue, drooling and sternal recumbency. The muscle paralysis is progressive; it usually begins at the hindquarters and gradually moves to the front limbs, head and neck.

The shaker foal syndrome is usually seen in animals less than 4 weeks old. The most characteristic signs are a stilted gait, muscle tremors and the inability to stand for more than 4 to 5 minutes. Other symptoms may include dysphagia, constipation, mydriasis and frequent urination. In the later stages, foals usually develop tachycardia and dyspnea. Death generally occurs 24 to 72 hours after the initial symptoms and results from respiratory paralysis. Some foals are found dead without other clinical signs.

Pigs

Pigs are relatively resistant to botulism. Reported symptoms include anorexia, refusal to drink, vomiting, pupillary dilation and muscle paralysis.

Foxes and Mink

During outbreaks of botulism, many animals are typically found dead, while others have various degrees of paralysis and dyspnea. The clinical picture is similar in commercially raised foxes.

Birds

In poultry and wild birds, flaccid paralysis is usually seen in the legs, wings, neck and eyelids. Wildfowl with paralyzed necks may drown. Broiler chickens with the toxicoinfectious form may also have diarrhea with excess urates.

Communicability

Botulism is not communicable by casual contact but, in some cases, tissues from dead animals can be toxic if ingested by other animals.

Diagnostic Tests

Botulism can be difficult to diagnose, as the toxin is not always found in clinical samples or the feed. Diagnosis is often a matter of excluding other diseases. A definitive diagnosis can be made if botulinum toxin is identified in the feed, stomach or intestinal contents, vomitus or feces. The toxin is occasionally found in the blood in peracute cases. Botulinum toxin can be detected by a variety of techniques, including enzyme–linked immunosorbent assays (ELISAs), electrochemiluminescent (ECL) tests and mouse inoculation or feeding trials. The toxins can be typed with neutralization tests in mice.

In toxicoinfectious botulism, the organism can be cultured from tissues. C. botulinum is an anaerobic, Gram positive, spore–forming rod. On egg yolk medium, toxin–producing colonies usually display surface iridescence that extends beyond the colony. The iridescent zone around the colony is usually larger for C, D and E toxins.

Treatment and Vaccination

The treatment is usually supportive and may include gastric lavage to remove some of the toxin. Botulinum antitoxin is sometimes used in animals; the success rate may depend on the type of toxin causing the disease and the species of animal. Type C antitoxins have been effective in some outbreaks in birds and mink. There are also some reports of success with guanidine hydrochloride. Antibiotics are used in the toxicoinfectious form, but are not always successful in birds.

In endemic areas, vaccines can be used in horses, cattle, sheep, goats, mink and pheasants. In chickens, they may not be cost–effective.

Morbidity and Mortality

Botulism is common in wild waterfowl; an estimated 10 to 50 thousand wild birds are killed annually. In some large outbreaks, a million or more birds may die. Ducks appear to be affected most often. Botulism also affects commercially raised poultry. In chickens, the mortality rate varies from a few birds to 40% of the flock. Some affected birds may recover without treatment.

Botulism seems to be relatively uncommon in most domestic mammals; however, in some parts of the world, epidemics with up to 65% morbidity are seen in cattle. The prognosis is poor in large animals that are recumbent. In cattle, death generally occurs within 6 to 72 hours after sternal recumbency. Most dogs with botulism recover within 2 weeks.

Post–Mortem Lesions

There are no pathognomonic lesions; the lesions are usually the result of general muscle paralysis. Respiratory paralysis may cause nonspecific signs in the lungs. In shaker foal syndrome, the most consist lesions are excess pericardial fluid with strands of fibrin, pulmonary edema and congestion. Foreign material in the fore–stomachs or stomach may suggest botulism.

Internet Resources

Animal Health Australia.
The National Animal Health Information System (NAHIS)
http://www.brs.gov.au/usr–bin/aphb/ahsq?dislist=alpha

Bacteriological Analytical Manual Online
http://www.cfsan.fda.gov/~ebam/bam–toc.html

Centers for Disease Control and Prevention (CDC)
http://www.cdc.gov/ncidod/dbmd/diseaseinfo/botulism_t.htm

Manual on meat inspection for developing countries
http://www.fao.org/docrep/003/t0756e/t0756e00.htm

Material Safety Data Sheets–Canadian Laboratory Center for Disease Control http://www.hc–sc.gc.ca/pphb–dgspsp/msds–ftss/index.html#menu

Medical Microbiology
http://www.gsbs.utmb.edu/microbook

The Merck Manual
http://www.merck.com/pubs/mmanual/

The Merck Veterinary Manual
http://www.merckvetmanual.com/mvm/index.jsp

USAMRIID's *Medical Management of Biological Casualties Handbook*
http://www.vnh.org/BIOCASU/toc.html

U.S. FDA Foodborne Pathogenic Microorganisms and Natural Toxins Handbook (Bad Bug Book)
http://vm.cfsan.fda.gov/~mow/intro.html

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Brucellosis

Malta Fever, Mediterranean Fever, Undulant Fever
Enzootic Abortion, Contagious Abortion, Bang's Disease

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Etiology

Brucellosis results from infection by various species of *Brucella*, a Gram negative, facultative intracellular rod in the family Brucellaceae. Six species occur in humans and animals: *Brucella abortus*, *B. melitensis*, *B. suis*, *B. ovis*, *B. canis* and *B. neotomae*. *B. abortus* usually causes brucellosis in cattle, bison and water buffalo. *B. melitensis* is the most important species in sheep and goats, and *B. suis* in pigs. *B. ovis* can cause infertility in rams. *B. neotomae* is found in American wood rats. In humans, brucellosis can be caused by *B. abortus*, *B. melitensis*, *B. suis* and, rarely, *B. canis*. The vaccines for *B. abortus* and *B. melitensis* are also pathogenic for humans.

Seven biovars have been identified for *B. abortus,* three for *B. melitensis* and five for *B. suis*. *B. suis* biotype 4 was formerly known as *B. rangiferi*.

Geographic Distribution

Brucellosis is found worldwide but is well controlled in most developed countries. Clinical disease is still common in Africa, the Middle East, Central and Southeast Asia, South America and some Mediterranean countries.

Brucella species vary in their geographic distribution. *B. melitensis* is particularly common in Latin America, central Asia, the Mediterranean, and around the Arabian Gulf. This species does not seem to occur in northern Europe, Southeast Asia, Australia or New Zealand. It is rare in the United States. *B. ovis* is seen in Australia, New Zealand and many other sheep-raising regions, including the United States. *B. suis* can be found worldwide, but the infection rate is high only in parts of South America and Southeast Asia, and in feral pigs in Australia and the southeastern United States. *B. abortus* has been eradicated from Japan, Canada, northern Europe, Australia and New Zealand. In humans, brucellosis is rare in Europe, Canada and United States but occurs regularly in the Middle East, the Mediterranean, Mexico and Central America.

Transmission

Among animals, *Brucella* is usually transmitted by contact with the placenta, fetus, fetal fluids and vaginal discharges from infected animals. Animals are infectious after either an abortion or full term parturition. Bacteria can also be found in the blood, urine, milk and semen; shedding in milk and semen can be prolonged or lifelong. Infection occurs by ingestion and through mucous membranes, broken skin and possibly intact skin. The mammary gland can be infected by direct contact; in cattle, the udder can be colonized by *B. abortus*, *B. melitensis* or *B. suis* on the hands of farm workers. *B. suis*, *B. ovis* and *B. canis* can be spread venereally; venereal transmission of *B. abortus* can occur but is rare. Some *Brucella* species can be transmitted vertically.

Humans become infected by ingestion or through the mucous membranes and breaks in the skin. Brucellosis is sometimes spread by raw milk and unpasteurized cheese. In abattoirs and in the laboratory, *Brucella* can probably be transmitted by aerosols. *B. canis* is rare in humans; infections are thought to occur only after frequent close contact.

Brucella can be spread on fomites. In conditions of high humidity, low temperatures and no sunlight, these organisms can remain viable for several months in water, aborted fetuses, manure, wool, hay, equipment and clothes. *Brucella* is destroyed by several hours of exposure to direct sunlight.

Disinfection

Brucella is susceptible to 1% sodium hypochlorite, 70% ethanol, iodine/alcohol solutions, glutaraldehyde and formaldehyde. Bacteria can also be inactivated by moist heat (121°C for a minimum of 15 min) or dry heat (160 to 170°C for a minimum of an hour).

Infections in Humans

Incubation Period

The incubation period is difficult to determine in humans but has been estimated at 5 days to several months. Most infections seem to become apparent after 2 to 4 weeks. Aerosolization of bacteria in biological weapons could result in a shorter incubation period.

Clinical Signs

Asymptomatic infections are common in humans. In symptomatic cases, the disease is extremely variable and the clinical signs may appear insidiously or abruptly. Some cases of brucellosis resemble influenza; the symptoms may include fever, headache, generalized weakness, malaise, sweating, fatigue and severe limb or back pains. Coughing and pleuritic chest pain are occasionally seen. Gastrointestinal signs, including anorexia, nausea, vomiting, diarrhea and constipation occur frequently in adults but less often in children. Irritability, insomnia, mental depression and emotional instability sometimes develop.

In many patients, the symptoms last for 2 to 4 weeks and are followed by spontaneous recovery. Others develop an intermittent fever, with symptoms recurring and receding at 2- to 14- day intervals. Most people with this undulant form recover completely in 3 to 12 months. A few patients become chronically ill, with symptoms of chronic fatigue, depressive episodes and arthritis. Relapses can be seen months after the initial symptoms, even in successfully treated cases. Hypersensitivity reactions can mimic the symptoms of brucellosis.

Occasional complications include arthritis, endocarditis, granulomatous hepatitis, meningitis, uveitis, orchitis, cholecystitis, osteomyelitis and other bone lesions. Rare cases of encephalitis, peripheral neuropathy, radiculoneuropathy and meningovascular syndromes have also been reported.

Communicability

Brucellosis is not usually transmitted from person to person. Rarely, bacteria have been spread in tissue transplants and by sexual contact.

Diagnostic Tests

A presumptive diagnosis can be made by identifying the characteristic organisms with a modified acid-fast stain. The definitive diagnosis is by culture or serology. PCR techniques may also be available. *Brucella* species can sometimes be isolated from the blood early in the infection; bone marrow is often positive at this stage. Occasionally, bacteria can be recovered from the cerebrospinal fluid, urine or tissues.

In humans, most infections are diagnosed by serology. Serologic tests include serum agglutination, a modified Coombs' (antiglobulin) technique, ELISAs and immunoblotting (Western blotting). Serologic diagnosis is complicated by previous exposures and other factors. Chronic brucellosis can be extremely difficult to diagnose, if the serologic results are equivocal and the organism cannot be cultured.

Treatment and Vaccination

Antibiotics are usually the mainstay of treatment; long-term treatment may be required. Some forms of localized disease, such as endocarditis, may require surgery. Vaccines have not been developed for humans.

Morbidity and Mortality

Brucellosis is usually an occupational disease; most cases occur in abattoir workers, veterinarians, hunters, farmers and livestock producers. In rural areas, children are sometimes infected after drinking raw milk or eating unpasteurized cheese. Human brucellosis is rare in the United States; the annual incidence is 0.5 cases per 100,000 persons. The incidence is much higher in some other parts of the world, particularly in southwest Asia; in Kuwait, the annual incidence is up to 128 cases per 100,000 persons.

Many infections are asymptomatic but symptomatic infections can be prolonged, with slow recovery and a small possibility of complications. Increased numbers of symptomatic infections could be seen after a biological attack with aerosolized bacteria. The mortality rate is low; in untreated persons, estimates of the case fatality rate vary from less than 2% to 5%. Deaths are usually caused by endocarditis or meningitis.

Infections in Animals

Species Affected

Most species of *Brucella* are associated with a limited number of hosts, but infections can occur in other species, particularly when they are kept in close contact. *Brucella abortus* is found in cattle, bison and water buffalo and occasionally in sheep, goats and dogs. *B. melitensis* is the most important cause of brucellosis in sheep and goats. It occasionally occurs in cattle and dogs. *B. suis* infects domestic and feral pigs. Some biovars can infect reindeer, caribou, hares, mice, Arctic foxes, wolves, rodents and occasionally cattle and dogs. *B. ovis* is seen in sheep, *B. canis* in dogs and *B. neotomae* in American wood rats. Horses can develop fistulous withers or poll evil from *Brucella abortus* and occasionally *B. suis*. *Brucella* species have also been found in deer, bison, elk, coyotes, camels, moose, hares, chickens and desert rats.

Incubation Period

Systemic signs are not generally seen after infection. The period between infection and reproductive signs is

variable. In cattle, abortions and stillbirths usually occur 2 weeks to five months after infection.

Clinical Signs

Brucellosis in cattle

In cattle, *B. abortus* causes abortions, stillbirths and weak calves; abortions usually occur during the second half of gestation. The placenta may be retained and lactation may be decreased. Testicular abscesses are sometimes seen in bulls. Arthritis can develop after long-term infections. Systemic signs do not usually occur.

Brucellosis in sheep and goats

In sheep and goats, *B. melitensis* can cause abortion, retained placenta, orchitis and epididymitis. Abortions usually occur late in gestation in sheep and during the fourth month of gestation in goats. In goats, mastitis and lameness may be seen. Arthritis is rare in sheep.

B. ovis affects sheep but not goats. This organism can cause epididymitis, orchitis and impaired fertility in rams. Initially, only poor quality semen may be seen; later, lesions may be palpable in the epididymis and scrotum. The testes may atrophy permanently. Abortions, placentitis and perinatal mortality can be seen but are uncommon. Systemic signs are rare.

Brucellosis in pigs

In pigs, the most common symptom is abortion, which can occur at any time during gestation, and weak or stillborn piglets. Vaginal discharge is often minimal and the abortions may be mistaken for infertility. Temporary or permanent orchitis can be seen in boars. Boars can also excrete *B. suis* asymptomatically in the semen and sterility may be the only sign of infection. Swollen joints and tendon sheaths or lameness can occur in both sexes. Less common signs include posterior paralysis, metritis, and abscesses in other parts of the body. Although some pigs recover, others remain permanently infected. Fertility can be permanently impaired.

Brucellosis in horses

In horses, *B. abortus* and occasionally *B. suis* can cause inflammation of the supraspinous or supra-atlantal bursa; this syndrome is known, respectively, as fistulous withers or poll evil. The bursal sac becomes distended by a clear, viscous, straw-colored exudate and develops a thickened wall. It can rupture, leading to secondary inflammation. In chronic cases, nearby ligaments and the dorsal vertebral spines may become necrotic. *Brucella*-associated abortions are rare in horses.

Brucellosis in dogs

B. canis causes abortions, stillbirths and infertility in dogs. Most infections are seen in kennels. Abortions usually occur during the last trimester and are followed by a prolonged vaginal discharge. Infected dogs may have lymphadenitis, epididymitis, periorchitis and prostatitis. Fever is not usually seen.

Communicability

Yes. Bacteria are present in the placenta, fetal fluids, fetus, vaginal discharges, milk, semen and urine. Infectious bacteria are also found in the bursa of horses with poll evil or fistulous withers. Some animals, particularly ruminants, can shed bacteria long-term or lifelong.

Diagnostic Tests

Brucellosis can be diagnosed by culture, serology or other tests. Some serologic tests are not useful in some hosts or for some species of *Brucella*.

Microscopic examination

A presumptive diagnosis can be made if the characteristic organisms are found in abortion products, vaginal discharges, milk, semen or various tissues by modified acid-fast staining. *Brucella* is an aerobic, nonmotile, Gram negative coccobacillus or short rod. Bacteria are usually found singly, but are occasionally seen in pairs or small groups. Direct examination may not detect the small numbers of organisms present in milk and dairy products.

Culture

Brucella species can be recovered from numerous tissues, particularly fetal membranes, vaginal secretions, milk, semen, arthritis or hygroma fluids, and the stomach contents, spleen and lung from aborted fetuses. In carcasses, bacteria can sometimes be isolated from the lymph nodes, spleen, uterus, udder, testis, epididymis, joint exudate, abscesses and other tissues. Repeated sampling of the semen may be necessary in *B. ovis* infections, as this organism is shed intermittently. Blood can be cultured from dogs; this species can be bacteremic for as long as 18 months after infection.

A wide variety of media can be used for culture; suitable media include Trypticase soy agar, modified Thayer-Martin medium, Farrell's medium, serum dextrose agar, glycerol dextrose agar and Castañeda's medium. In a four-day old culture, colonies of the smooth form viewed through a transparent medium are a pale honey color, 1-2 mm in diameter, translucent and round, with smooth margins. The colonies are convex and pearly white when seen from above. In the rough form, the colonies are much less transparent and have a more granular, dull, matte white to brown surface. In nature, *Brucella abortus*, *B. melitensis*, *B. suis* and *B. neotomae* usually occur in the smooth form; *B. ovis* and *B. canis* are found in the rough form. Identification to the genus level is by biochemical tests and slide agglutination. The species and

biovar can be identified by phage lysis and cultural, biochemical and serological characteristics.

Serology

Brucellosis is often diagnosed by serology. In cattle, agglutination tests are used to detect antibodies in serum, milk, whey and semen. The most commonly used tests are the buffered *Brucella* antigen tests (BBAT), also known as the card and plate agglutination tests. Tube agglutination tests may also be used. An enzyme-linked immunosorbent assay (ELISA) is available for milk or serum. The milk ring test can be used to screen bulk milk samples for *B. abortus*. Other, less commonly used, serologic tests include complement fixation, rivanol precipitation and acidified antigen procedures. Fluorescence polarization tests are being developed.

In sheep and goats, *B. melitensis* can be diagnosed with BBAT or complement fixation. ELISAs are being developed. The bulk milk ring test is not used in small ruminants. *B. ovis* infections can be diagnosed by ELISA, complement fixation, hemagglutination inhibition, indirect agglutination and gel diffusion tests.

The tube or slide agglutination and gel diffusion tests are generally used in dogs. Nonspecific agglutination sometimes occurs but can be eliminated by pretreatment with 2-mercaptoethanol.

Serology is less reliable in pigs. Conventional serologic tests can misdiagnose *B. suis* infections in individual pigs; these tests are considered to be more reliable for a herd diagnosis. The BBATs are used most often; complement fixation or other serum agglutination tests may also be available. ELISA techniques and fluorescence polarization assays have been developed and may be more effective than other serologic tests.

Other tests

Immunofluorescent techniques can detect *B. abortus* in the placenta and fetus or *B. ovis* in the semen. A brucellin allergic skin test is sometimes used to test pigs for *B. suis* or unvaccinated sheep and goats for *B. melitensis*. This assay is generally a herd test. Polymerase chain reaction (PCR) techniques have also been developed for some species.

Treatment and Vaccination

There is no practical treatment for infected cattle or pigs, but long-term antibiotic treatment is sometimes successful for *B. canis* infections in dogs. Antibiotics can eliminate *B. ovis* infections in valuable rams but the fertility may remain poor. In horses with fistulous withers or poll evil, the infected bursa may need to be surgically removed.

Commercial vaccines are available for cattle, sheep and goats. A *B. ovis* vaccine is manufactured in New Zealand and some other counties but is not available in the United States. Successful vaccines have been difficult to develop for pigs; this species is generally not vaccinated except in China. No vaccines are made for dogs. Vaccines have not been successful in preventing fistulous withers or poll evil in horses.

Morbidity and Mortality

Morbidity can be high in naïve animals. In cattle, *B. abortus* can spread rapidly in an unvaccinated, naïve herd; 80% of cattle in late gestation may abort. In dogs, up to 75% fewer puppies may be weaned from affected kennels. In pigs, the abortion rate is 0 to 80%. Ruminants usually abort only during their first gestation, but abortions can occur repeatedly in affected dogs. Fertility can be permanently impaired after infections with some species of *Brucella*. Deaths are not usually seen in adult animals.

Post-Mortem Lesions

In ruminants, the fetus may be autolyzed, normal or have evidence of bronchopneumonia. In cattle, acute or chronic placentitis is sometimes seen. The cotyledons may be red, yellow, normal or necrotic. The intercotyledonary region is typically leathery, with a wet appearance and focal thickening. Placentitis, with edema and necrosis of the cotyledons and a thickened and leathery intercotyledonary region, can also be seen in sheep infected with *B. melitensis*. The placenta is usually normal in goats. Fetal and placental lesions are rare in pigs infected with *B. suis*, but the fetus may be autolyzed.

At slaughter, granulomatous inflammatory lesions may be found in the reproductive tract, mammary gland, supramammary lymph nodes and joints of adult animals.

Internet Resources

Animal Health Australia.
The National Animal Health Information System (NAHIS)
http://www.brs.gov.au/usr-bin/aphb/ahsq?dislist=alpha

Brucellosis in Sheep and Goats (Brucella melitensis)
European Commission Health and Consumer Protection Directorate General
http://europa.eu.int/comm/food/fs/sc/scah/out59_en.pdf

Centers for Disease Control and Prevention (CDC)
http://www.cdc.gov/ncidod/dbmd/diseaseinfo/brucellosis_t.htm

FAO Manual on meat inspection for developing countries
http://www.fao.org/docrep/003/t0756e/t0756e00.htm

Material Safety Data Sheets–
Canadian Laboratory Center for Disease Control
http://www.hc-sc.gc.ca/pphb-dgspsp/msds-ftss/

index.html#menu

Medical Microbiology

http://www.gsbs.utmb.edu/microbook

Office International des Epizooties (OIE)

Manual of Standards for Diagnostic Tests and Vaccines

http://www.oie.int/eng/normes/mmanual/a_summry.htm

The Merck Manual

http://www.merck.com/pubs/mmanual/

The Merck Veterinary Manual

http://www.merckvetmanual.com/mvm/index.jsp

USAMRIID's Medical Management of Biological Casualties Handbook

http://www.vnh.org/BIOCASU/toc.html

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Eastern Equine Encephalomyelitis, Western Equine Encephalomyelitis and Venezuelan Equine Encephalomyelitis

"Sleeping Sickness"

Eastern Equine Encephalomyelitis –EEE, Eastern equine encephalitis, Eastern encephalitis

Western Equine Encephalomyelitis –WEE, Western equine encephalitis

Venezuelan Equine Encephalomyelitis –VEE, VE, Peste loca, Venezuelan equine encephalitis, Venezuelan encepha - litis, Venezuelan equine fever

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Etiology

Eastern, Western and Venezuelan equine encephalomyelitis result from infection by the respectively named viruses in the genus *Alphavirus* (family Togaviridae). In the human literature, the disease is usually called Eastern, Western or Venezuelan equine encephalitis.

Eastern Equine Encephalomyelitis Virus

There are two variants of the Eastern equine encephalomyelitis (EEE) virus. The virus found in North America is more pathogenic than the variant that occurs in South and Central America. The Eastern equine encephalitis virus can cause disease in humans, horses and some species of birds.

Western Equine Encephalomyelitis Viruses

The Western equine encephalomyelitis (WEE) virus group includes the Western equine encephalitis (WEE), Sindbis, Ft. Morgan, Aura and Y 61–33 viruses. The Western equine encephalitis virus can cause disease in humans, horses and some species of birds. A related virus, the Highlands J virus, is sometimes isolated in the eastern United States. The Highlands J virus can cause disease in turkeys. It has also been linked to a single case of encephalitis in a horse.

Venezuelan Equine Encephalomyelitis Viruses

The Venezuelan equine encephalomyelitis (VEE) complex contains at least 8 viral subtypes; these viruses are divided into epizootic and enzootic groups. The epizootic subtypes are responsible for most epidemics. They are highly pathogenic for horses and also cause illness in humans. Enzootic (sylvatic) subtypes are generally found in limited geographic areas, where they occur in natural cycles between rodents and mosquitoes. The enzootic subtypes can cause human disease. They are usually non-pathogenic for horses; however, in 1993 an enzootic variant was responsible for an outbreak of VEE among horses in Mexico.

Geographic Distribution

The Western, Eastern and Venezuelan encephalomyelitis viruses are found in North, Central and South America. The WEE viruses occur in western Canada, Mexico, parts of South America, and west of the Mississippi in the United States. The EEE virus is found in eastern Canada, all states east of the Mississippi, Arkansas, Minnesota, South Dakota and Texas. It also occurs in the Caribbean and regions of Central and South America, particularly along the Gulf coast. VEE viruses are endemic in South and Central America and Trinidad. Enzootic subtypes of VEE are also found in Florida, the Rocky Mountains and northern plains of the United States. Most epidemics of VEE occur in northern and western South America, but some may spread into adjacent countries, including the United States.

Transmission

Eastern and Western Equine Encephalomyelitis

The Eastern and Western encephalomyelitis viruses are transmitted mainly by mosquitoes. Normally, these two viruses cycle between birds and mosquitoes. Humans and horses are incidental, dead end hosts.

The EEE virus can be isolated from 27 species of mosquitoes in the United States. *Culiseta melanura*, a mosquito that primarily feeds on birds, is the most important vector in the enzootic cycle. During some years, the virus is spread to mammalian hosts by bridge vectors (mosquitoes that feed on both birds and mammals) such as *Coquilletidia perturbans*, *Aedes canadensis*, *Aedes sollicitans*, *Aedes vexans* and *Culex nigripalpus*. WEE cycles between passerine birds and culicine mosquitoes. *Culex tarsalis* appears to be the most important vector; other significant vectors include *Aedes melanimon*, *Aedes dorsalis* and *Aedes campestris*. The EEE and WEE viruses may be transmitted vertically in mosquitoes.

In birds, EEE and WEE are occasionally spread by non–arthropod–borne routes. During outbreaks of disease in game birds, infections are introduced by mosquitoes but spread in the flock mainly by feather picking and cannibalism. EEE and WEE viruses do not survive outside the host.

Venezuelan Equine Encephalomyelitis

The Venezuelan equine encephalomyelitis viruses are also spread mainly by mosquitoes. The enzootic subtypes of VEE cycle between rodents and mosquitoes, mainly *Culex* species. Birds may also be involved in some cycles. Humans and horses are incidental hosts.

The natural host for the epizootic subtypes, between epidemics, is unknown. Horses infected with the epizootic subtypes can infect mosquitoes and are the main amplifiers for VEE during epidemics. Other mammals, including cattle, pigs and dogs, can be infected but do not usually become ill or spread the virus. Many different species of mosquitoes and other hematogenous insects can transmit epizootic VEE. Efficient vectors include arthropods in the genera *Aedes*, *Anopheles*, *Culex*, *Deinocerites*, *Mansonia*, *Haemogogus*, *Sabethes* and *Psorophora*.

In some cases, humans have also developed VEE after being exposed to debris from the cages of infected laboratory rodents. Person–to–person transmission has not been reported; however, the VEE virus can be found in pharyngeal secretions in humans and is stable when aerosolized. The virus can also occur in dried blood and exudates.

Disinfection

EEE and WEE viruses do not persist in the environment but the VEE virus may be found in dried blood and exudates. VEE, EEE and WEE are susceptible to many disinfectants including 1% sodium hypochlorite, 70% ethanol, 2% glutaraldehyde and formaldehyde. They can also be destroyed by moist or dry heat, as well as drying.

Infections in Humans

Incubation Period

In humans, the incubation period is usually 1 to 6 days for VEE and 4 to 15 days for WEE and EEE.

Clinical Signs

Eastern and Western Equine Encephalitis

Eastern equine encephalitis usually begins abruptly, with fever, myalgia and headache and sometimes nausea and vomiting. This prodrome is often followed by neurologic signs; the symptoms may include confusion, focal neurologic deficits, somnolence, neck stiffness, stupor, disorientation, coma, tremors, seizures and paralysis. Abdominal pain, diarrhea and a sore throat can also occur. The mortality rate for EEE is high.

Western equine encephalitis resembles EEE but is usually asymptomatic or mild in adults, with nonspecific signs of illness and few deaths. The symptoms usually appear abruptly and may include fever, headache, nausea, vomiting, anorexia and malaise. Many adults do not develop other symptoms. In more severe cases, neurologic symptoms, similar to those seen in EEE, can develop. WEE can be severe in children, particularly infants under a year of age.

Venezuelan Equine Encephalitis

In humans, VEE is usually an acute, often mild, systemic illness. The clinical signs may include fever, generalized malaise, severe headache, photophobia and myalgia, particularly in the legs and lum*bos*acral region. These symptoms usually last for 24 to 72 hours and may be followed by a cough, sore throat, nausea, vomiting and diarrhea. The disease usually lasts 1 to 2 weeks. In pregnant women, VEE can affect the fetus; fetal encephalitis, placental damage, abortion or severe congenital neurologic anomalies may be seen.

Encephalitis usually develops in 4% of children and less than 1% of adults. In mild cases, the symptoms may include lethargy, somnolence, or mild confusion. Severe infections are characterized by seizures, ataxia, paralysis or coma. An increased incidence of encephalitis would be expected after a biological attack with aerosolized viruses.

Communicability

WEE and EEE viruses are not found in the blood or cerebrospinal fluid after the symptoms appear, and only low titers develop during the viremic phase. These viruses do not seem to be spread directly from person to person. Humans do not transmit EEE or WEE viruses to mosquitoes.

Person–to–person transmission is theoretically possible for VEE, but has not been reported in natural cases. Humans with VEE can infect mosquitoes for approximately 72 hours.

Diagnostic Tests

Eastern, Western and Venezuelan equine encephalitis can be diagnosed by virus isolation, serology or other tests. In humans, VEE virus can be isolated from blood, cerebrospinal fluid or throat swabs. Serology is also useful; a rise in titer or the presence of specific IgM is diagnostic. A variety of serologic tests may be available, including virus neutralization, ELISA, hemagglutination inhibition and complement fixation. Indirect immunofluorescence assays have been developed for VEE. Polymerase chain reaction (PCR) or immunohistochemistry may be available at some laboratories.

During the febrile stage of the illness, antigen–capture ELISAs can often detect VEE antigens in the blood. This test is generally not useful during the encephalitic stage. PCR assays may also be available.

Treatment and Vaccination

Treatment consists of supportive care. Investigational VEE, EEE and WEE vaccines may be available for humans at high risk of infection. The VEE vaccine may not be effective for all of the VEE complex viruses.

Morbidity and Mortality

Eastern Equine Encephalitis

In the United States, approximately 12 to 17 cases of EEE are reported to the Centers for Disease Control and Prevention (CDC) each year. The infection rate is approximately 33% and the morbidity rate 90%. Most cases are seen in people over 55 and children younger than 15. Eastern equine encephalitis is often severe in humans. Estimates of the case fatality rate vary from 33 to 70% and permanent neurologic deficits can occur in survivors.

Western Equine Encephalitis

The annual incidence of WEE is highly variable; during an epidemic in 1941, over 3000 human cases occurred in the United States and Canada. The case–infection ratio is approximately 1:1000 in adults, 1:58 in children from 1 to 4 years old and 1:1 in infants up to a year of age. The overall mortality rate is 3 to 4%. Most infections in adults are asymptomatic or mild, without neurologic disease. Infections in children, particularly infants under one year old, can be severe. Approximately 5 to 30% of young patients have permanent neurologic damage.

Venezuelan Equine Encephalomyelitis

In natural epidemics of VEE, human cases are usually preceded by an epidemic in horses. After an attack by a biological weapon, cases would be expected simultaneously in both species or first in humans. Caution should be used in interpreting such patterns of infection, as VEE may be missed in wild or free–ranging equines.

Humans are highly susceptible to VEE; approximately 90 to 100% of exposed individuals become infected and nearly 100% of these infections are symptomatic. However, most infections are mild. Less than 1% of adults develop encephalitis and approximately 10% of these cases are fatal. The overall case fatality is less than 1%. Very young or elderly patients are more likely to develop severe infections. Encephalitis occurs in approximately 4% of children less than 15 years old; the case fatality rate in children with neurologic disease is 35%. A higher incidence of neurologic disease could be seen in adults as well as children after a biological attack with aerosolized virus; mortality rates would be expected to be correspondingly higher.

Infections in Animals

Species Affected

The equine encephalomyelitis viruses usually cause illness only in equine species and humans. These viruses can also infect a variety of other animals, often asymptomatically.

Eastern and Western Equine Encephalomyelitis

Eastern equine encephalitis virus infects horses, pigs, birds, bats, reptiles, amphibians, forest–dwelling marsupials and rodents. WEE virus can infect birds, horses and a variety of mammals. Most WEE and EEE infections in birds are asymptomatic; however, disease can be seen in chukar partridges, pheasants, psittacine birds, ratites and whooping cranes.

Venezuelan Equine Encephalomyelitis

Rodents seem to be the natural hosts for the enzootic subtypes of VEE but, in some cases, birds may also be involved. VEE virus can cause serious disease in horses, mules, burros and donkeys. Cattle, pigs and dogs can be infected asymptomatically. VEE can also infect a wide variety of laboratory animals.

Incubation Period

The incubation period for WEE or EEE is 5 to 14 days. The clinical signs of VEE are usually seen 1 to 5 days after infection.

Clinical Signs

Eastern and Western Equine Encephalomyelitis in Horses

Eastern and Western equine encephalomyelitis are very similar in horses. The initial clinical signs are usually fever, anorexia and depression. In severe cases, this prodromal stage is followed by neurologic signs; the symptoms may include involuntary muscle movements, impaired vision, aimless wandering, head pressing, circling, an inability to swallow, ataxia, paresis, paralysis and convulsions. Periods of excitement or intense pruritus can also be seen. Laterally recumbent animals may develop a characteristic “paddling” motion. Both EEE and WEE can also cause asymptomatic infections or mild disease without neurologic signs. Occasional cases of encephalitis have been seen in pigs.

Venezuelan Equine Encephalomyelitis in Horses

The enzootic subtypes usually infect horses subclinically. The epizootic subtypes can cause asymptomatic infections or two clinical syndromes. One syndrome resembles EEE and WEE; in this form, a febrile prodrome is followed by neurologic signs and sometimes diarrhea

and colic. Death can occur within hours after the onset of neurologic signs or after protracted disease. Animals that recover may have permanent neurologic signs. The second form of VEE is a generalized acute febrile disease without neurologic signs. The symptoms may include fever, weakness, depression, anorexia, colic and diarrhea.

Western and Eastern Equine Encephalitis Viruses in Birds

Western and Eastern equine encephalomyelitis virus infections are asymptomatic in most species of birds, but fatal infections can occur in some species. Most reported outbreaks have been caused by EEE. Chukar infected with the EEE virus are usually dull and listless, with ruffled feathers. The birds are typically found sitting on their hocks with the beak on the ground. In pheasants, the symptoms may include incoordination, weakness and progressive paralysis. In the late stages of the disease, the birds cannot stand but can still move their wings. Whooping cranes may develop lethargy, ataxia and paresis of the legs and neck. The EEE virus has also been isolated from psittacine birds with viral serositis.

Both EEE and WEE viruses can cause fatal hemorrhagic enteritis in ratites; the characteristic clinical signs include depression, hemorrhagic diarrhea, and vomiting of bloodstained material. Highlands J and EEE infections can also cause depression, somnolence, decreased egg production and increased mortality in turkeys.

Communicability

Birds can amplify the Western and Eastern equine encephalomyelitis viruses and are infectious for mosquitoes. Horses are dead–end hosts for these viruses. Direct transmission has been seen only between birds.

Both horses and birds infected with the VEE virus are infectious for mosquitoes. In horses, the virus can be found in bodily fluids. Some authorities suggest that transmission may be possible by direct contact or aerosols but natural transmission between horses or from horses to humans has not been seen. Humans can be infected by laboratory rodents.

Diagnostic Tests

Eastern and Western Equine Encephalomyelitis

In horses, Eastern and Western equine encephalomyelitis can be diagnosed by serology. Tests include plaque reduction neutralization (PRN), hemagglutination inhibition, antibody–capture enzyme linked immunosorbent assay (ELISA) and complement fixation. Cross–reactions may occur between EEE and WEE antibodies in the complement fixation and hemagglutination inhibition tests.

Clinical infections in birds are usually diagnosed by virus isolation. In horses, virus isolation is useful in cases of EEE; it is rarely successful in WEE. The EEE virus can usually be recovered from the brain of infected horses; other tissues such as the liver or spleen may also be positive. EEE and WEE viruses can be isolated in newborn mice, embryonating chicken eggs, newly hatched chicks or cell cultures including primary chicken or duck embryo fibroblasts, African green monkey kidney (Vero), rabbit kidney (RK–13), and baby hamster kidney (BHK–21) cells. Virus identity can be confirmed by complement fixation, immunofluorescence or plaque reduction neutralization (PRN) tests. EEE viruses can also be detected in the brain with immunohistochemistry or an antigen–capture ELISA.

Venezuelan Equine Encephalomyelitis

VEE can be diagnosed by virus isolation or serology. VEE virus can often be recovered from the blood during the febrile stage and is sometimes isolated from the brain of animals with encephalitis. Virus is also found occasionally in the pancreas or other tissues. Animals with neurologic signs are not usually viremic. VEE virus can be isolated in guinea pigs, hamsters, mice, embryonated chicken eggs or cell lines including Vero, RK–13, BHK–21 and duck or chicken embryo fibroblasts. The virus can be identified by complement fixation, hemagglutination inhibition, plaque reduction neutralization (PRN) or immunofluorescence assays. Subtypes can be characterized by immunofluorescence, differential PRN tests or nucleic acid sequencing.

VEE can also be diagnosed by serology. Serologic tests include the PRN test, complement fixation, hemagglutination inhibition and ELISAs. Cross–reactions can occur between VEE, EEE and WEE viruses in the hemagglutination inhibition test. Animals may have pre–existing antibodies to enzootic variants of VEE.

Treatment and Vaccination

Treatment consists of supportive care. Equine vaccines are available for EEE, WEE and VEE. EEE vaccines are also available for susceptible birds, but do not always prevent disease.

Morbidity and Mortality

Eastern and Western Equine Encephalomyelitis

WEE often occurs as sporadic cases of encephalitis in horses, scattered over a wide area. Clinical cases of EEE are usually more clustered. EEE is often fatal in horses; the mortality rate is 50 to 90%. WEE is more likely to be asymptomatic or mild, with mortality rates of approximately 20 to 30%. Significant morbidity and mortality can also occur in poultry, game birds and ratites. In pheasants and other susceptible species of birds, both the morbidity and mortality rates may be up to 90%. The morbidity and mortality rates for emus with hemorrhagic enteritis can be greater than 85%.

Venezuelan Equine Encephalomyelitis

Most enzootic VEE subtypes do not result in serious disease or deaths in horses. Epizootic subtypes can cause significant morbidity and mortality; the morbidity rate can be as high as 90% and the mortality rate varies from 30 to 90%.

Post–Mortem Lesions

The gross lesions are usually nonspecific. In horses with VEE, the lesions in the central nervous system vary from no lesions to extensive necrosis with hemorrhages. Necrotic foci are sometimes seen in the pancreas, liver and heart of horses with VEE. Congestion of the brain and meninges is found in some cases of EEE and WEE. Antemortem trauma can result in ecchymotic hemorrhages.

Microscopic analysis of the brain tissue is often diagnostic. The typical lesion is severe inflammation of the gray matter; neuronal degeneration, infiltration by inflammatory cells, gliosis, perivascular cuffing and hemorrhages may be seen. WEE, EEE and VEE can sometimes be differentiated by the location and pattern of the lesions in the brain.

Internet Resources

Animal Health Australia.
The National Animal Health Information System (NAHIS)
http://www.brs.gov.au/usr–bin/aphb/ahsq?dislist=alpha

Centers for Disease Control and Prevention (CDC)
http://www.cdc.gov/ncidod/dvbid/arbor/arbdet.htm

Manual for the Recognition of Exotic Diseases of Livestock
http://panis.spc.int/

Material Safety Data Sheets –Canadian Laboratory Center for Disease Control http://www.hc–sc.gc.ca/pphb–dgspsp/msds–ftss/index.html#menu

Medical Microbiology
http://www.gsbs.utmb.edu/microbook

Office International des Epizooties (OIE)

Manual of Standards for Diagnostic Tests and Vaccines
http://www.oie.int/eng/normes/mmanual/a_summry.htm

The Merck Manual
http://www.merck.com/pubs/mmanual/

The Merck Veterinary Manual
http://www.merckvetmanual.com/mvm/index.jsp

USAMRIID's Medical Management of Biological Casualties Handbook
http://www.vnh.org/BIOCASU/toc.html

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Glanders

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Etiology

Glanders results from infection by *Burkholderia mallei*, a Gram negative, aerobic, nonmotile rod (family Pseudomonadaceae). This organism was formerly known as *Pseudomonas mallei* and is closely related to the agent of melioidosis, *Burkholderia pseudomallei*.

Geographic Distribution

Glanders is seen in some Middle Eastern countries, the Indian subcontinent, Southeast Asia, parts of China and Mongolia, and Africa. Sporadic cases are also seen in South America. Cross–reactions with *B. pseudomallei* may interfere with serologic estimates of the prevalence and distribution of *B. mallei*.

Transmission

Infectious organisms are found in skin exudates and respiratory secretions. Latently infected horses can also spread the disease. Transmission is usually by ingestion in horses and related species; the infection can also be spread by inhalation or through skin abrasions and the conjunctiva. Carnivores can become infected after eating contaminated meat. *B. mallei* is spread on fomites, including harnesses, grooming tools, food and water troughs. This organism can survive in room temperature water for as long as 30 days and may be able to survive for a few months in other favorable environments. It is susceptible to heat, light, drying and a variety of chemicals.

Humans can become infected after contact with sick animals or infectious materials. Transmission is typically through small wounds and abrasions in the skin; ingestion or inhalation, with invasion through the mucous membranes, is also possible. Cases are usually seen in people who handle laboratory samples or have frequent close contact with horses, mules and donkeys. Natural human infections are rare even when infection rates in horses are 5–30%. Weaponization of *B. mallei* has been attempted by some countries.

Disinfection

Burkholderia mallei is susceptible to numerous disinfectants including benzalkonium chloride, iodine, mercuric chloride in alcohol, potassium permanganate, 1% sodium hypochlorite, 70% ethanol and 2% glutaraldehyde. It is less susceptible to phenolic disinfectants. This organism can also be destroyed by heating to 55°C for 10 min or by ultraviolet irradiation.

Infections in Humans

Incubation Period

In natural infections, the incubation period is 1 to 14 days. Infections from aerosolized forms in biological weapons are expected to have an incubation period of 10–14 days.

Clinical Signs

Humans can develop four forms of disease: septicemia, pulmonary infection, acute localized infection or chronic infection. Combinations of syndromes can occur.

In the septicemic form, fever, chills, myalgia, and pleuritic chest pain develop acutely. Other symptoms may include generalized erythroderma, jaundice, photophobia, lacrimation, diarrhea and granulomatous or necrotizing lesions. Tachycardia, cervical adenopathy and mild hepatomegaly or splenomegaly may also be seen. Death usually occurs in 7 to 10 days.

The pulmonary form is characterized by symptoms of pneumonia, pulmonary abscesses and pleural infusions. A cough, fever, dyspnea and mucopurulent discharge may be seen. Skin abscesses sometimes develop after several months.

Localized infections are characterized by nodules, abscesses and ulcers in the mucous membranes, skin, lymphatic vessels and/or subcutaneous tissues. A mucopurulent, blood–tinged discharge may be seen from the mucous membranes. The

lymph nodes may be swollen. Mucosal or skin infections can disseminate; symptoms of disseminated infections include a papular or pustular rash, abscesses in the internal organs (particularly the liver and spleen) and pulmonary lesions. Disseminated infections are associated with septic shock and high mortality.

In the chronic form, multiple abscesses, nodules or ulcers can be seen in the skin, liver, spleen or muscles.

Communicability

Person to person transmission has been reported, but appears to be uncommon. Human epidemics have not been seen.

Diagnostic Tests

Glanders can be diagnosed by isolation and identification of *Burkholderia mallei*. In the septicemic form, blood cultures may be negative until just before death. *B. mallei* is a nonmotile Gram negative rod; organisms from young cultures and clinical samples are rods with bipolar staining, while bacteria from older cultures can be pleomorphic. Few bacteria may be found in clinical samples. On blood agar or Loeffler's serum agar, colonies are approximately 1 mm, white, semitranslucent and viscid. Older colonies turn yellow. On glycerin–potato media, a clear honey–like layer is seen by day 3; this eventually darkens to reddish–brown or brown. *B. mallei* can also be isolated by inoculation into guinea pigs. A polymerase chain reaction can differentiate *B. mallei* DNA from *B. pseudomallei*.

Serology is sometimes helpful; serologic tests include agglutination tests and complement fixation. High background titers can be found in normal serum and cross–reactions may occur with Burkholderia pseudomallei, the causative agent of Melioidosis Positive reactions in agglutination tests develop only after 7 to 10 days.

Treatment and Vaccination

B. mallei is variably susceptible to antibiotics. Long–term treatment or multiple drugs may be necessary. Treatment may be ineffective, particularly in cases of septicemia; the bacteria produce toxins. No vaccine is available.

Morbidity and Mortality

In most parts of the world, naturally acquired cases of glanders are rare and sporadic. Infections are typically seen in people who work with clinical samples or have frequent, close contact with horses. Human epidemics have not been seen.

The septicemic form of glanders has a high mortality rate in humans: the case fatality rate is 95% in untreated cases and more than 50% when the infection is treated. The mortality rate for localized disease is 20% when treated. The overall mortality rate is 40%.

Infections in Animals

Species Affected

The major hosts are horses, mules and donkeys. Infections can also occur in dogs, cats, goats and camels; cats may be particularly susceptible. Hamsters and guinea pigs can be infected in the laboratory.

Incubation Period

In natural infections, the incubation period varies from 6 days to many months; 2 to 6 weeks is typical. Experimental infections can result in clinical signs after 3 days.

Clinical Signs

Acute, chronic and latent forms of glanders are seen in horses, mules and donkeys.

The clinical signs in the acute form may include a high fever, cough, inspiratory dyspnea, a thick nasal discharge, and deep, rapidly spreading ulcers on the nasal mucosa. Healed ulcers become star–shaped scars. The submaxillary lymph nodes are usually swollen and painful, and the lymphatic vessels on the face may be thickened. Secondary skin infections, with nodules, ulcers and abscesses may be seen. Affected animals usually die within 1 to 2 weeks.

The chronic form develops insidiously. The symptoms may include coughing, malaise, unthriftiness, weight loss and an intermittent fever. A chronic purulent nasal discharge may be seen, often only from one nostril. Other symptoms may include ulcers and nodules on the nasal mucosa, enlarged submaxillary lymph nodes, chronic enlargement and induration of lymphatics and lymph nodes, swelling of the joints and painful edema of the legs. The skin may contain nodules, particularly on the legs, that rupture and ulcerate. This form is slowly progressive and may be fatal.

In the latent form, there may be few symptoms other than a nasal discharge and occasional labored breathing. Lesions may be found only in the lungs.

Communicability

Horses, donkeys and mules can transmit the disease to other animals and humans; nasal discharges and wound exudates are infectious. Laboratory samples are highly infectious to humans.

Natural transmission from infected animals to humans appears to be inefficient. Despite infection rates of 30% in horses in China during World War II and 5–25% in Mongolia, few or no human cases occurred.

Diagnostic Tests

Glanders can be diagnosed by bacteriologic isolation of *B. mallei*, inoculation into guinea pigs, the mallein test or serology.

In live animals, *B. mallei* is isolated from skin lesions or blood samples. Organisms are much easier to find in fresh than in old lesions, where they may be scant. At necropsy, bacteria can also be isolated from exudates in the nasal passages and the upper respiratory tract. *B. mallei* is a nonmotile Gram negative rod; bacteria from young cultures and clinical samples are rods with bipolar staining while organisms from older cultures may be pleomorphic. On blood agar or Loeffler's serum agar, colonies are approximately 1 mm, white, semitranslucent and viscid. Older colonies turn yellow. On glycerin–potato media, a clear honey–like layer is seen by day 3; this eventually darkens to reddish–brown or brown. A polymerase chain reaction can differentiate *B. mallei* DNA from *B. pseudomallei*.

In the mallein test, a positive reaction is indicated by eyelid swelling 1 to 2 days after intrapalpebral injection of a protein fraction of *B. mallei*, or by conjunctivitis after administration in eyedrops.

A variety of serologic tests are available, including complement fixation, enzyme–linked immunosorbent assay (ELISA), indirect hemagglutination, counter–immunoelectrophoresis and immunofluorescence. The most accurate and reliable tests in horses are complement fixation and ELISA. Agglutination and precipitin tests are unreliable for horses with chronic glanders and animals in poor condition. Complement fixation tests cannot be used with donkey or mule serum.

Treatment and Vaccination

Antibiotics may be effective; however, treatment is not generally recommended, as infections can be spread to humans and other animals, and treated animals may become asymptomatic carriers. Vaccines are not available.

Morbidity and Mortality

Glanders can spread widely when large numbers of animals are in close contact; in China, 30% of horses were infected when large numbers of animals were gathered together in World War II. Acute infections are usually fatal within 1 to 2 weeks. Animals with the chronic form can sometimes survive for years.

Post–Mortem Lesions

At necropsy, there may be ulcers, nodules and stellate scars in the nasal cavity, trachea, pharynx, larynx, skin and subcutaneous tissues. Catarrhal bronchopneumonia with enlarged bronchial lymph nodes may be evident. The lungs, liver, spleen and kidneys may contain firm, rounded, encapsulated miliary gray nodules similar to tubercles. The lymphatic vessels may be swollen; the lymph nodes are typically enlarged and fibrotic and contain focal abscesses. In addition, necrosis may be noted in the internal organs and testes.

Internet Resources

Animal Health Australia.
The National Animal Health Information System (NAHIS)
http://www.brs.gov.au/usr–bin/aphb/ahsq?dislist=alpha

Centers for Disease Control and Prevention (CDC)
http://www.cdc.gov/ncidod/dbmd/diseaseinfo/glanders_t.htm

"Glanders and Melioidosis" in *eMedicine*
http://www.*emedicine*.com/emerg/topic884.htm

FAO Manual on meat inspection for developing countries
http://www.fao.org/docrep/003/t0756e/t0756e00.htm

Foreign Animal Diseases.
United States Animal Health Association
http://www.vet.uga.edu/vpp/gray_book/FAD

Manual for the Recognition of Exotic Diseases of Livestock
http://panis.spc.int/

Material Safety Data Sheets –Canadian Laboratory Center for Disease Control
http://www.hc–sc.gc.ca/pphb–dgspsp/msds–ftss/index.html#menu

Office International des Epizooties (OIE)

Manual of Standards for Diagnostic Tests and Vaccines
http://www.oie.int/eng/normes/mmanual/a_summry.htm

The Merck Veterinary Manual
http://www.merckvetmanual.com/mvm/index.jsp

USAMRIID's Medical Management of Biological Casualties Handbook
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Melioidosis

Pseudoglanders, Whitmore Disease

Last Updated: Jan. 2004

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Etiology

Melioidosis results from infection by *Burkholderia pseudomallei*, a motile Gram negative bacillus (family Pseudomonadaceae). This organism was formerly known as *Pseudomonas pseudomallei*.

Geographic Distribution

Melioidosis is endemic in Southeast Asia, Africa, Australia, the Middle East, India and China. This infection is mainly associated with tropical and subtropical regions; however, *B. pseudomallei* has also been isolated from the temperate regions of southwest Australia and France. Isolated cases have occurred in South America and in the states of Hawaii and Georgia in the United States. *B. pseudomallei* is generally found in water or moist soil.

Transmission

New infections are primarily acquired from organisms in the environment. Contaminated swamps, muddy water and rodents are important sources of infection. Soil-borne infections are generally associated with heavy rainfall or flooding in areas with high humidity or temperatures. Infection can occur by ingestion, inhalation, or through wounds and abrasions. The role of insect bites is uncertain. Direct human-to-human and animal-to-human transmission is rare but can occur after contact with blood or body fluids. Depending on the site of the infection, contaminated body fluids may include urine, nasal secretions and milk. Shed organisms can survive for months in soil and water.

Disinfection

B. pseudomallei can survive for months to years in soil and water, but can be readily destroyed by heat. Moist heat of 121°C for at least 15 min or dry heat of 160-170°C for at least 1 hour is recommended for disinfection. The organism is also susceptible to numerous disinfectants, including 1% sodium hypochlorite, 70% ethanol, glutaraldehyde and formaldehyde.

Infections in Humans

Incubation Period

In natural infections, the incubation period can vary from two days to months or years. Infections may remain latent for years. Infections from aerosolized forms in biological weapons are expected to have an incubation period of 10-14 days.

Clinical Signs

B. pseudomallei infections may be inapparent or can result in pulmonary infections, disseminated septicemia, acute nondisseminated septicemia or localized chronic suppurative infections.

The most serious form is disseminated septicemic infection. In natural infections, this form is most common in people with pre-existing debilitating diseases such as AIDS, cancer, diabetes and kidney failure. Its onset may be acute. The clinical signs may include severe headache, severe dyspnea, disorientation, pharyngitis, upper abdominal pain, diarrhea, pustular skin lesions and notable muscle tenderness. Pulmonary signs and symptoms of arthritis or meningitis are sometimes seen. This form is often accompanied by septic shock.

Pulmonary infections vary in severity, from mild bronchitis to severe necrotizing pneumonia. Symptoms can appear suddenly or gradually and may include fever, headache, cough, tachypnea, rales, blood-tinged sputum, anorexia, generalized myalgia and dull aching or pleuritic chest pain.

Localized chronic suppurative infections are characterized by abscesses in the skin, lymph nodes or other organs including the brain. Osteomyelitis is common with this form. Fever may or may not be present. Acute nondisseminated septicemic infection also occurs, involves a single organ and is relatively rare.

In cases with acute infection of the oral, nasal or conjunctival mucosa, the clinical signs may include mucopurulent, blood streaked nasal discharge from the nose, as well as nodules and ulcerations in the septum and turbinates.

Communicability

Yes. Direct transmission between humans or from humans to animals is rare but can occur after contact with blood or body fluids. Depending on the site of the infection, contaminated body fluids may include urine, nasal secretions and milk. Human carriers have not been seen.

Diagnostic Tests

Melioidosis can be diagnosed by isolation and identification of *Burkholderia pseudomallei*. Bacteria may be found in blood, sputum, tissues and wound exudates. In the septicemic form, blood cultures may be negative until just before death.

The organism has a wrinkled colony form, which may be mixed with smooth colonies. A characteristic odor has been described. (Due to the risk of infection, directly sniffing the plates is not recommended.) Organisms are oval, Gram negative bacilli, with bipolar staining in young cultures. A polymerase chain reaction can differentiate *B. mallei* DNA from *B. pseudomallei*.

Serologic tests on paired sera may be helpful. High single titers in the presence of clinical signs may also be used for diagnosis. Serologic tests include agglutination tests, indirect hemagglutination, complement fixation, immunofluorescence assays and enzyme immunoassays. Cross-reactions may occur in serologic tests with *Burkholderia mallei*, the causative agent of glanders.

Treatment and Vaccination

B. pseudomallei is variably susceptible to antibiotics. Long-term treatment may be necessary and multiple drugs may be needed. Pulmonary resection or draining of abscesses is sometimes necessary for chronic cases. No vaccine is available.

Morbidity and Mortality

In natural infections, the mortality rate is usually less than 10%, except in disseminated septicemic infections; mortality rates as high as 90% may be seen in this form. Localized lesions may be progressive or disseminate. Fatal infections are more common in patients who are immunosuppressed or have concurrent disease.

Exposure to biological weapons containing aerosolized forms is expected to result in septicemia or severe pulmonary infections, with high mortality rates in spite of treatment.

Infections in Animals

Species Affected

Infection with *B. pseudomallei* is seen most often in pigs, goats and sheep. It occurs less often in cattle, horses, dogs, rodents, birds, dolphins, tropical fish, primates and various wild animals. Hamsters, guinea pigs and rabbits can be infected in the laboratory.

Incubation Period

The incubation period can vary from days to months or years. Abscesses may be carried without symptoms.

Clinical Signs

B. pseudomallei infection results in suppurating or caseous lesions in lymph nodes or other organs. Infections may be asymptomatic and abscesses may be found in clinically normal goats, sheep and pigs. Symptomatic melioidosis mimics other diseases; the clinical signs vary with the site of the lesion. They may include fever, loss of appetite, and lymphadenopathy, often involving the submandibular nodes in pigs. Lameness or posterior paresis, nasal discharge, encephalitis, gastrointestinal symptoms or respiratory signs may also be seen in some species. Extensive abscesses and infections of vital organs can be fatal.

In sheep and goats, lung abscesses and pneumonia are common. Other common symptoms in sheep include high fever, coughing, ocular and nasal discharge, lameness with swollen joints, neurologic disease, and gradual emaciation. Some animals may display only weakness and fever. Mastitis is sometimes seen in goats and the superficial lymph nodes and udder may contain palpable abscesses. Pulmonary lesions in goats are usually less severe than in sheep and coughing is not prominent. In horses, neurologic disease, respiratory symptoms, or colic and diarrhea have been described. Infections in pigs are usually chronic and asymptomatic. Acute infections in this species may result in septicemia with fever, anorexia, coughing and nasal and ocular discharges. Abortions and stillbirths may occur but are rare, and orchitis may occur in boars. Cattle are rarely affected, but may develop pneumonia or neurologic signs.

Communicability

Yes. Direct transmission between animals or from animals to humans is rare but can occur after contact with blood or body fluids. Depending on the site of the infection, contaminated body fluids may include urine, nasal secretions and milk. Animals may become carriers.

Diagnostic Tests

Swabs of nasal discharges and samples collected from lesions should be submitted for culture. Organisms may be isolated from the sputum, blood, wound exudates

or tissues. In some species, serum may also be collected for serologic tests.

Melioidosis is diagnosed by isolation and identification of *Burkholderia pseudomallei*. This organism has a wrinkled colony form, which may be mixed with smooth colonies. A characteristic odor has been described. (Due to the risk of infection, directly sniffing the plates is not recommended.) Organisms are oval, Gram negative bacilli, with bipolar staining in young cultures. A polymerase chain reaction can differentiate *B. mallei* DNA from *B. pseudomallei*.

In some species, agglutination tests, indirect hemagglutination, immunofluorescence, and enzyme immunoassays can be used for diagnosis. Cross-reactions may occur in serologic tests with *Burkholderia mallei*, the causative agent of glanders.

Treatment and Vaccination

B. pseudomallei is susceptible to various antibiotics, but relapses can occur when treatment is stopped. Vaccines are available in some countries but are not effective against large challenge doses.

Morbidity and Mortality

Mortality varies with the site of the lesions, but can be high in sheep. Extensive abscesses and infections of vital organs can be fatal. Disseminated septicemic infections have a high mortality rate, but are less common in animals than humans. Infections may be progressive.

Post-Mortem Lesions

At necropsy, the major findings are multiple abscesses containing thick, caseous greenish-yellow or off-white material. These abscesses are generally not calcified. The regional lymph nodes, spleen, lung, liver and subcutaneous tissues are most often involved, but abscesses can occur in most organs. In acute cases, pneumonic changes in the lungs, meningoencephalitis and suppurative polyarthritis may be found. In cases with suppurative arthritis, the joints may contain fluid and large masses of greenish-yellow purulent material.

In sheep, common findings include abscesses and suppuration in the nasal mucosa. Splenic abscesses are often found in pigs at slaughter.

Internet Resources

Material Safety Data Sheets–
Canadian Laboratory Center for Disease Control
http://www.hc-sc.gc.ca/pphb-dgspsp/msds-ftss/index.html#menu

Manual for the Recognition of Exotic Diseases of Livestock

http://panis.spc.int/

Centers for Disease Control and Prevention (CDC)

http://www.cdc.gov/ncidod/dbmd/diseaseinfo/melioidosis_g.htm

The Merck Manual

http://www.merck.com/pubs/mmanual/

The Merck Veterinary Manual

http://www.merckvetmanual.com/mvm/index.jsp

Animal Health Australia.
The National Animal Health Information System (NAHIS)

http://www.brs.gov.au/usr-bin/aphb/ahsq?dislist=alpha

USAMRIID's Medical Management of Biological Casualties Handbook

http://www.vnh.org/BIOCASU/toc.html

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Plague

Peste, Black Death, Bubonic Plague, Pneumonic Plague, Septicemic Plague, Pestis Minor

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Etiology

Plague results from infection by *Yersinia pestis*, a non–motile, facultatively intracellular, Gram negative rod (family Enterobacteriaceae).

Geographic Distribution

Plague is seen in parts of North and South America, Africa, the Middle East, Central and Southeast Asia and Indonesia. Foci of infection are found in the former Soviet Union. This disease does not occur in Europe, Australia or Japan.

Transmission

Plague is usually spread between rodents or humans by the bites of infected fleas. Vectors include a variety of rodent fleas, particularly the oriental rat flea (*Xenopsylla cheopis*). In the U.S., the most common vector is *Oropsylla montana*, a flea often found on California ground squirrels, rock squirrels, and sometimes other rodents including prairie dogs. Human fleas (*Pulex irritans*) may also carry *Y. pestis*. *Y. pestis* is also present in the tissues and body fluids of infected animals; these bacteria can be transmitted directly through mucous membranes and broken skin. Aerosols from people or animals with the pneumonic form are infectious and animals may transmit bacteria in bites. Carnivores often become infected when they eat diseased rodents.

In the wild, *Y. pestis* is maintained in cycles between wild rodents and fleas; sporadic cases occur in humans and domestic animals when they come into contact with infected animals or fleas. Infection of rodents in urban areas, particularly the Roof rat or Norway rat, can result in epizootic and epidemic plague in humans. Direct person–to–person transmission can occur in pneumonic plague.

Y. pestis can survive for long periods of time in organic material; it may remain viable for up to 100 days in blood and for as long as 9 months in human bodies. Infectious bacteria can also be found in water, moist soil and grains for several weeks. *Y. pestis* is not resistant to desiccation or heat: it is destroyed by exposure to 55°C for 15 minutes or several hours in sunlight.

Disinfection

Y. pestis is susceptible to a number of disinfectants including 1% sodium hypochlorite, 70% ethanol, 2% glutaraldehyde, formaldehyde and iodine–based and phenolic disinfectants. It can also be inactivated by moist heat (121° C for at least 15 min) or dry heat (160–170° C for at least 1 hour).

Infections in Humans

Incubation Period

The incubation period for pneumonic plague is 1 to 3 days. The symptoms of bubonic plague appear after 2 to 6 days.

Clinical Signs

Three major forms of plague are seen in humans: bubonic plague, septicemic plague, pneumonic plague.

Bubonic plague appears acutely; the initial symptoms may include fever, headache, malaise and myalgia. Vomiting, nausea, abdominal pain, hepatomegaly and splenomegaly are sometimes seen. Patients with bubonic plague typically develop an infected, swollen, and very painful draining lymph node, called a bubo; the bubo is often one of the femoral or inguinal lymph nodes. Other lymph nodes, or multiple nodes, may also be involved. In some cases, a pustule, vesicle, eschar or papule occurs at the site of the flea bite.

Bubonic plague can develop into septicemic plague. Bacteremia is present in most cases of bubonic plague but the symptoms of septicemia – including high fever, chills, malaise, nausea, vomiting, abdominal pain, diarrhea and hypotension – do not always develop. Meningitis is relatively rare; it occurs in approximately 6% of people with the septicemic or pneumonic forms. Thrombo*s*es in blood vessels can cause necrosis and

gangrene of the extremities or disseminated intravascular coagulation (DIC).

Pneumonic plague occurs after inhalation of bacteria or after blood–borne spread to the lungs. Pneumonic plague is expected to be the predominant form in a bioterrorist attack. The symptoms of pneumonic plague develop acutely and include high fever, chills, headache, myalgia and malaise. Nausea, vomiting, diarrhea and abdominal pain may be seen. Within 24 hours, a cough with bloody sputum develops; the sputum contains only specks of blood at first but eventually becomes foamy and pink or red. Cervical buboes occur rarely. Pneumonic plague is rapidly fatal, with dyspnea, stridor and cyanosis ending in respiratory failure and circulatory collapse.

Pestis minor is a benign form of bubonic plague, usually seen only in regions where plague is endemic. Pestis minor is characterized by fever, lymphadenitis, headache and prostration. These symptoms resolve spontaneously within a week.

Communicability

In the United States, person–to–person transmission of bubonic plague has not occurred since 1924; however, person–to–person transmission is seen in epidemics in some countries. Pneumonic plague can be highly contagious, particularly under crowded conditions

Diagnostic Tests

A presumptive diagnosis can be made by identifying the characteristic organisms in sputum, blood, lymph node (bubo) aspirates or cerebrospinal fluid; *Y. pestis* is a Gram negative, non–motile, facultative intracellular coccobacillus with bipolar staining. Organisms can be identified by immunofluorescence. Immunoassays can also detect *Y. pestis* antigens in serum. Polymerase chain reaction (PCR) assays are used in research. Bacteriophage typing can be helpful in tracing outbreaks.

Plague can also be diagnosed by isolation of *Y. pestis*. Organisms can be recovered from sputum, blood or aspirates of lymph nodes and may be cultured on ordinary media including blood agar, MacConkey agar or infusion broth. Automated systems may misidentify this bacterium, as it grows slowly and biochemical reactions may be delayed. Guinea pig inoculation can also be used.

Serology is occasionally helpful. A fourfold rise in titer is diagnostic. Latex agglutination is most often used, but passive hemagglutination tests and complement fixation are also available.

Treatment and Vaccination

Antibiotics are effective in the early stages of bubonic or pneumonic plague; in pneumonic plague, their efficacy is often limited after 24 hours. Buboes are occasionally drained but usually resolve with antibiotic treatment.

Vaccines may be available for people with occupational risk factors; these vaccines are not wholly protective, particularly against the pneumonic form. A whole cell vaccine was marketed until November 1998 but appears to have been taken off the market. A new vaccine is in development and may be more effective against both forms of plague.

Morbidity and Mortality

The mortality rate is approximately 50 to 60% for untreated bubonic plague and nearly 100% for untreated pneumonic plague. The pneumonic form is often fatal within 48 hours after it becomes symptomatic. Early treatment reduces the mortality rate to less than 5%; however, treatment for the pneumonic form must be started during the first 24 hours after symptoms begin.

Worldwide, approximately 1,000 to 2,000 cases of plague are seen annually; epidemics occur regularly in Africa and Asia. Sporadic cases also occur in North and South America after exposure to wild rodents and fleas. In the United States, approximately 18 cases of plague were seen yearly during the 1980s; the mortality rate for these cases was approximately 14%.

Infections in Animals

Species Affected

More than 200 species of mammals can be infected with *Y. pestis*. Rodents are the reservoir hosts. Many rodents, including prairie dogs, chipmunks, wood rats, ground squirrels, deer mice and voles suffer occasional epidemics or maintain the virus in natural cycles. Rock squirrels and the California ground squirrel are often the sources of human infections in the United States. Rats are usually the carriers for epidemics in humans. Rabbits, wild carnivores, domestic cats and dogs can develop plague when they are exposed to infected rodents or their fleas; among carnivores, cats are particularly susceptible.

Incubation Period

Clinical signs develop can develop within 3–4 days in experimentally infected cats.

Clinical Signs

Asymptomatic infections and mild illness are typical in some reservoir hosts. Wild carnivores including coyotes, skunks and raccoons can also seroconvert without clinical disease. Other animals may have fever, lymphadenitis, abscesses in internal organs, or sudden death from sepsis.

In cats, clinical signs can include fever, anorexia, dehydration and depression. Infected cats may develop enlarged lymph nodes near the site of infection: the submandibular or cervical lymph nodes are most often involved. Infected lymph nodes can develop abscesses, ulcerate and drain. Swellings may also be seen around the

head, neck and eyes. Sneezing, hemoptysis, incoordination, quadriplegia, necrotic tonsillitis and symptoms of pneumonia may occur.

Dogs seem to be relatively resistant to plague and animals may seroconvert without symptoms. High fevers and lymphadenopathy, with occasional deaths, have also been seen. Ten experimentally infected dogs developed a fever and other signs of illness but recovered spontaneously during the next week.

Communicability

Yes. Bacteria can be transmitted in aerosols, by direct contact with tissues and body fluids, and in bites. Infected fleas can transmit bacteria for months.

Diagnostic Tests

Plague can be diagnosed by isolation of *Y. pestis*; bacteria may be found in blood, nasal swabs, lymph node aspirates, transtracheal aspirates and tissue samples. If neurologic signs are present, cerebrospinal fluid (CSF) may yield bacteria. *Y. pestis* is a Gram negative, non–motile, facultative intracellular coccobacillus with bipolar staining. The organism can be identified by immunofluorescence or antigen–capture enzyme linked immunosorbent assays (ELISAs).

Organisms can also be cultured; *Y. pestis* will grow on ordinary media including blood agar, MacConkey agar or infusion broth. Automated systems may misidentify this bacterium, as it grows slowly and biochemical reactions may be delayed. Guinea pig inoculation can also be used. A rise in titer in paired serum samples is diagnostic, if the animal survives; the latex hemagglutination and passive hemagglutination tests (PHA) are often used.

Treatment and Vaccination

Early treatment with antibiotics can be successful.

Morbidity and Mortality

In endemic areas, many rodents – including chipmunks, wood rats, ground squirrels, deer mice and voles – suffer occasional epidemics. Mortality in some rodent species can be high; infections are fatal in nearly 100% of prairie dogs. Between outbreaks, bacteria seem to cycle in reservoir populations without causing high mortality

The mortality rate is 50% in cats fed plague–infected mice; sick cats may die within 1 to 2 days or after several weeks. Dogs, coyotes, raccoons, skunks and other carnivores often seroconvert without symptoms; clinical infections and deaths are relatively rare in these species. Ten experimentally infected dogs recovered spontaneously.

Post–Mortem Lesions

Post mortem lesions vary with the type of infection. Signs can include lymphadenopathy, bacterial pneumonia with lung hemorrhages, and necrosis in the liver, spleen and other internal organs.

Internet Resources

Centers for Disease Control and Prevention (CDC) Plague Pages

http://www.bt.cdc.gov/agent/plague/index.asp

Material Safety Data Sheets–Canadian Laboratory Center for Disease Control
http://www.hc–sc.gc.ca/pphb–dgspsp/msds–ftss/index.html#menu

Medical Microbiology

http://www.gsbs.utmb.edu/microbook

The Merck Manual

http://www.merck.com/pubs/mmanual/

The Merck Veterinary Manual

http://www.merckvetmanual.com/mvm/index.jsp

USAMRIID's Medical Management of Biological Casualties Handbook

http://www.vnh.org/BIOCASU/toc.html

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Psittacosis

Avian Chlamydiosis, Ornithosis, Parrot Fever

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Etiology

In birds, avian chlamydiosis results from infection by *Chlamydophila psittaci* (order Chlamydiales, family Chlamydiaceae). Psittacosis is the human disease caused by infection with *Chlamydophila psittaci*. This organism, previously known as *Chlamydia psittaci*, is a Gram negative, coccoid, obligate intracellular bacterium. There are at least six avian serotypes.

Geographic Distribution

Avian chlamydiosis can be found worldwide. *C. psittaci* is particularly common in psittacine birds in tropical and subtropical regions. This disease is present in the United States. In a 1982 survey, *C. psittaci* was isolated from 20–50% of necropsied pet birds in California and Florida.

Transmission

Among birds, *C. psittaci* is transmitted frequently by inhalation of infectious dust and occasionally by ingestion. Fomites can also spread chlamydiosis, and biting insects, mites, and lice may be important in mechanical transmission. Birds can be asymptomatic carriers; carriers shed *C. psittaci* intermittently, particularly when stressed. One form of the organism, the elementary body, can survive in dried feces for months.

Humans usually become infected after inhaling contaminated dust from feathers or bird droppings. Direct contact with infected birds and bites can also spread the disease. Person–to–person transmission is rare but can occur by aerosol or venereal spread.

Disinfection

C. psittaci is susceptible to quaternary ammonium compounds, chlorophenols, iodophore disinfectants, formaldehyde, 80% isopropyl alcohol or a 1:100 dilution of household bleach.

Infections in Humans

Incubation Period

The incubation period in humans is 1 to 4 weeks; most infections become symptomatic after 10 days.

Clinical Signs

Psittacosis can be acute or insidious in onset. The disease varies from a mild, flu–like infection with a fever, chills, headaches, anorexia, malaise, sore throat and photophobia to a serious atypical pneumonia with dyspnea. There may be a dry cough, which sometimes becomes mucopurulent. In uncomplicated infections, the fever lasts for approximately 2 to 3 weeks then resolves. More rarely, a severe systemic illness with endocarditis, myocarditis and renal complications can develop. Hepatitis and neurologic complications including encephalitis, meningitis and myelitis have also been seen.

Communicability

Person–to–person transmission is rare; the agent is occasionally spread in aerosols during paroxysmal coughing. Venereal transmission has also been reported.

Diagnostic Tests

Psittacosis can be diagnosed by isolation of *C. psittaci* or by serology. *C. psittaci* can be isolated in embryonated eggs, laboratory animals, or cell cultures of buffalo green monkey (BGM), African green monkey (Vero), McCoy or L cells. Iodine staining of inclusion bodies or immunofluorescence can differentiate *C. psittaci* from *C. trachomatis*. DNA restriction endonuclease analysis can also distinguish these two organisms in tissue samples. Serologic tests include complement fixation or immunofluorescent tests; individuals treated with antibiotics may not develop antibodies. A presumptive diagnosis is sometimes made, based on exposure to birds and clinical signs.

Treatment and Vaccination

Antibiotics (tetracycline) combined with supportive care are effective. There is no vaccine.

Morbidity and Mortality

Currently, fewer than 50 confirmed cases are reported annually in the United States; additional undiagnosed or unreported cases are thought to occur. The disease may be mild or severe, depending on age and health of the individual and the extent of pneumonia; more serious disease is usually seen in the elderly and those who are debilitated. The mortality rate can be as high as 30% in severe infections left untreated; treated cases are rarely fatal. Convalescence may be slow after severe disease.

Infections in Animals

Species Affected

Avian chlamydiosis occurs in most birds, but is particularly common in psittacine birds, pigeons, doves, and mynah birds. This disease is sometimes seen in ducks and turkeys but only rarely in chickens.

Incubation Period

The incubation period in cage birds is usually three days to several weeks. However, in latent infections, active disease may be seen years after infection.

Clinical Signs

In turkeys, ducks, and pigeons, the clinical signs can include depression, ruffled feathers, weakness, inappetence, weight loss, nasal discharge, respiratory distress, yellowish–green or green diarrhea, and unilateral or bilateral conjunctivitis. Egg production is decreased. Nervous signs may be seen, including transient ataxia in pigeons and trembling or gait abnormalities in ducks.

In pet birds, common symptoms include anorexia, weight loss, diarrhea, yellowish droppings, sinusitis, respiratory distress, nervous signs, and conjunctivitis. Asymptomatic infections and mild infections with diarrhea or mild respiratory signs may also be seen. Residual disturbances in feathering may be apparent in survivors.

Communicability

Infected birds can shed *C. psittaci* for weeks to months. Shedding may be continuous or intermittent.

Diagnostic Tests

In live birds, avian chlamydiosis is usually diagnosed by isolating *C. psittaci* from pharyngeal or nasal swabs, feces, cloacal swabs, conjunctival scrapings or peritoneal exudate. At necropsy, the organism may be isolated from blood, ocular or nasal exudates, inflammatory exudates, or tissue samples from the lung, kidney, spleen, liver, and pericardium. If diarrhea is present, organisms may be found in the colonic contents or feces.

C. psittaci is isolated in embryonated eggs, laboratory animals or cell cultures of buffalo green monkey (BGM), African green monkey (Vero), McCoy or L cells. The organisms can be identified by direct immunofluorescence or other staining techniques. A single negative culture may be misleading, as carrier birds may shed *C. psittaci* only intermittently. Treatment with antibiotics during the 2 to 3 weeks before testing may also lead to false negatives.

Avian chlamydiosis can also be diagnosed by demonstrating *C. psittaci* in tissues, feces, or exudates by histochemical or immunohistochemical staining. Antigen capture enzyme–linked immunosorbent assays (ELISAs) are also used, but may lack sensitivity or cross–react with other Gram negative bacteria. Polymerase chain reaction (PCR) and polymerase chain reaction/ restriction fragment length polymorphism (PCR–RFLP) assays have been described.

Serology is occasionally helpful. At least a four–fold rise in titer should be seen in paired samples. Complement fixation is the standard test. Other assays include ELISA, latex agglutination (LA), elementary body agglutination (EBA), micro–immunofluorescence (MIFT), and agar gel immunodiffusion tests. The EBA test detects IgM only and can be used to diagnose current infections.

Treatment and Vaccination

Antibiotics are effective in treating the symptoms of avian chlamydiosis, but some birds may remain infected.

Morbidity and Mortality

Morbidity and mortality vary with the host species and pathogenicity of the serotype. Young birds tend to be more susceptible than older birds. In turkeys, serovar D strains cause 50–80% morbidity and 10–30% mortality. In broiler turkeys, up to 80% of infections with this serovar may be fatal. Other serovars in turkeys usually result in 5–20% morbidity, with mortality under 50%. In ducks, morbidity may be up to 80% and mortality 0–40%. Concurrent infections or stress increase the severity of the disease.

Post–Mortem Lesions

Post–mortem lesions in birds can include pneumonia, airsacculitis, hepatitis, myocarditis, epicarditis, nephritis, peritonitis, and splenitis. In turkeys, an enlarged and congested spleen may be the only lesion. Wasting, vascular congestion, fibrinous airsacculitis, fibrinous pericarditis, fibrinous pneumonia with congestion of the lungs, or fibrinous perihepatitis may also be seen. In pigeons, common lesions include hepatomegaly, airsacculitis, enteritis, and conjunctivitis with swollen and encrusted eyelids. The spleen may rupture. In cage

birds, the liver may be enlarged and yellow with focal necrosis. The spleen is often enlarged, with white foci. Airsacculitis, pericarditis, and congestion of the intestinal tract can also be seen.

Internet Resources

Centers for Disease Control and Prevention (CDC)

http://www.cdc.gov/ncidod/dbmd/diseaseinfo/psittacosis_t.htm

Material Safety Data Sheets–
Canadian Laboratory Center for Disease Control
http://www.hc–sc.gc.ca/pphb–dgspsp/msds–ftss/index.html#menu

Medical Microbiology

http://www.gsbs.utmb.edu/microbook

Office International des Epizooties (OIE)

Manual of Standards for Diagnostic Tests and Vaccines

http://www.oie.int/eng/normes/mmanual/a_summry.htm

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Q Fever

Query Fever

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Etiology

Q fever results from infection by *Coxiella burnetii*. This organism is an obligate intracellular pathogen and has been traditionally placed in the family Rickettsiaceae; however, recent phylogenetic studies have demonstrated that *C. burnetii* is more closely related to Legionella, Francisella and Rickettsiella in the gamma subdivision of Proteobacteria.

C. burnetii forms unusual spore–like structures that are highly resistant to environmental conditions. The organism also has two distinct antigenic phases. Phase I is pathogenic and is found in infected animals or in nature; phase II is less pathogenic and is recovered after bacteria are passaged repeatedly in cell cultures or eggs.

Geographic Distribution

Q fever has been found worldwide, except in New Zealand.

Transmission

C. burnetii can be transmitted by aerosols or direct contact; it is also spread by ingestion of an infected placenta, other reproductive discharges or milk. Organisms localize in the mammary glands, supramammary lymph nodes, uterus and placenta in domestic ruminants and other susceptible species; bacteria can be shed in milk, the placenta and reproductive discharges during subsequent pregnancies and lactations. *C. burnetii* can also be found in the feces and urine. Ticks seem to spread infections among ruminants and sometimes people. Transmission has occurred in blood transfusions and by sexual contact in humans. Organisms have also been found in the semen of bulls. Vertical transmission is possible but rare.

C. burnetii is highly resistant to environmental conditions and is easily spread by aerosols; infectious airborne particles can travel a half–mile or more. Viable organisms can be found for up to 30 days in dried sputum, 120 days in dust, 49 days in dried urine from infected guinea pigs, and for at least 19 months in tick feces. At 4–6°C, organisms can survive for 42 months in milk and 12 to 16 months in wool.

Disinfection

C. burnetii is highly resistant to physical and chemical agents. Variable susceptibility has been reported for hypochlorite, formalin and phenolic disinfectants; a 0.05% hypochlorite, 5% peroxide or 1:100 solution of Lysol® may be effective. *C. burnetii* is also susceptible to glutaraldehyde, ethanol, gaseous formaldehyde, gamma irradiation or temperatures of 130°C for 60 min. High temperature pasteurization destroys the organism.

Infections in Humans

Incubation Period

In humans, the incubation period varies from 2 to 40 days; the typical incubation period is approximately 2 to 5 weeks.

Clinical Signs

The symptoms of Q fever appear acutely and can include fever, chills, a severe headache, fatigue, malaise, myalgia and chest pains. The illness generally lasts from a week to more than 3 weeks. A nonproductive cough, with pneumonitis on X–ray, sometimes develops during the second week. In severe cases, lobar consolidation and pneumonia may occur; severe infections are particularly common in elderly or debilitated patients. Hepatitis is seen in approximately one third of patients with prolonged disease; the clinical signs may include fever, malaise, right upper abdominal pain, hepatomegaly and sometimes jaundice. In pregnant women, infections can result in premature delivery, abortion and placentitis.

Complications are not common but may include chronic hepatitis, aseptic meningitis, encephalitis, osteomyelitis, vasculitis and endocarditis. Endocarditis usually

occurs in people who have pre–existing damage to the heart valves. The symptoms are similar to subacute bacterial endocarditis.

Communicability

Person to person spread is very rare but has been seen in people with pneumonia.

Diagnostic Tests

In humans, Q fever is usually diagnosed by serology. Serologic tests can be done as early as the second week of illness; they may include immunofluorescence, ELISA, agglutination or complement fixation. Antibodies to the protein antigens found in phase II organisms appear in acute Q fever; antibodies to the lipopolysaccharide of phase I organisms indicate chronic Q fever. Organisms are occasionally found in stained tissue samples but this test is not routinely used in humans.

Isolation of *C. burnetii* is dangerous to laboratory personnel and is rarely done. Organisms can be recovered from blood samples; bacteria are isolated in cell cultures, embryonated chicken eggs or laboratory animals including mice, hamsters and guinea pigs. Blood cultures from patients with endocarditis are usually negative.

Treatment and Vaccination

Antibiotics can shorten the course of acute illness and reduce the risk of complications. Treatment of chronic cases is more difficult and may require long–term antibiotic therapy. Surgical replacement is sometimes necessary for damaged valves.

Effective vaccines may be available for people who are occupationally exposed. A licensed vaccine is available in Australia. In the United States, an investigational vaccine can be obtained from special laboratories such as the U.S. Army Medical Research Institute of Infectious Diseases (USAMRIID).

Morbidity and Mortality

Most cases of Q fever occur in people occupationally exposed to farm animals or their products: farmers, abattoir workers, researchers, laboratory personnel, dairy workers and woolsorters have an increased risk of infection. Approximately 60% of cases are thought to be asymptomatic. An additional 38% of infected people experience mild illness, while 2% develop severe disease and require hospitalization.

Q fever is usually a self–limiting illness; most cases resolve spontaneously within 2 days to 2 weeks. The mortality rate is 1% in untreated cases and lower in those who are treated. A biological attack with aerosolized organisms is expected to be similar to a natural outbreak.

Infections in Animals

Species Affected

Sheep, goats and cattle are the most common domestic animal reservoirs. Dogs, cats, rabbits, horses, pigs, camels, buffalo, rodents, pigeons, geese and other fowl may carry *C. burnetii*. Antibodies to *C. burnetii* have been found in badgers, coyotes, raccoons, opossums, badgers, jackrabbits, feral pigs, black bears and musk ox. Ticks and wild birds can also harbor this organism.

Incubation Period

The incubation period is variable; reproductive failure is usually the only symptom in animals. Abortions generally occur late in pregnancy.

Clinical Signs

Abortion, stillbirth, retained placenta, endometritis, infertility and small or weak offspring can be seen in ruminants, cats, dogs, rabbits and other species. Most abortions occur near term. Several abortions may be followed by uncomplicated recovery, particularly in small ruminants; in other cases, the disease may recur yearly.

With the exception of reproductive disease, animals are usually asymptomatic. Goats sometimes have a poor appetite and are depressed for 1 to 2 days before an abortion. Clinical signs including fever, anorexia, mild coughing, rhinitis and increased respiratory rates occur in experimentally infected sheep but have not been reported in natural infections. Experimentally infected cats develop fever and lethargy.

Communicability

Yes. Large numbers of organisms are found in the placenta, fetal fluids, aborted fetus, milk, urine and feces. Serologically negative animals may shed organisms.

Diagnostic Tests

C. burnetii can be detected in vaginal discharges, the placenta, placental fluids and aborted fetuses, as well as milk, urine and feces. Organisms are not shed continuously in milk and colostrum. In the placenta, organisms can be identified in exudates or areas of inflammation with a modified Ziehl–Neelsen or Gimenez stain; *C. burnetii* is an acid–fast, pleomorphic, small coccoid or filamentous organism. This organism is not usually detected by Gram stains. Bacterial identity can be confirmed by immunohistochemistry. Polymerase chain reaction techniques are also available in some laboratories. Fresh, frozen or paraffin–embedded samples of serum, buffy coat, milk, feces, vaginal exudates, cerebrospinal fluid, bone marrow, placenta, liver, cardiac valve, fetal tissue and other tissues can be tested by PCR.

A number of serologic tests are available; the most commonly used tests include indirect immunofluores-

cence, enzyme–linked immunosorbent assay (ELISA) and complement fixation. Cross–reactions have been seen between some strains of *C. burnetii* and Chlamydia in ELISA and immunoblot assays.

C. burnetii can be isolated in cell cultures, embryonated chicken eggs or laboratory animals including mice, hamsters and guinea pigs; however, isolation is dangerous to laboratory personnel and is rarely used for diagnosis.

Treatment and Vaccination

Little is known about the efficacy of antibiotic treatment in ruminants or other domestic animals. Treatment is sometimes recommended to reduce the risk of abortion. Antibiotics may in some cases suppress rather than eliminate infections. Isolating infected pregnant animals and burning or burying the reproductive membranes and placenta can decrease transmission.

Vaccines are not available for domestic ruminants in the United States but are used in other countries. Vaccines may prevent infections in calves, decrease shedding of organisms and improve fertility in infected animals. They do not eliminate shedding of the organism.

Morbidity and Mortality

Information on the prevalence of infection is limited. In an endemic region in California, 18 to 55% of sheep had antibodies to *C. burnetii*; the number of seropositive sheep varied seasonally and was highest soon after lambing. In other surveys, 82% of cows in some California dairies were seropositive, as well as 78% of coyotes, 55% of foxes, 53% of brush rabbits and 22% of deer in Northern California. In Ontario, Canada, infections were found in 33 to 82% of cattle herds and 0 to 35% of sheep flocks. Close contact with sheep appears to increase the risk of infection in dogs.

Significant morbidity can be seen in some species. In sheep, abortions can affect 5 to 50% of the flock. In one California study, Q fever may have been responsible for 9% of all abortions in goats. Deaths are rare in natural infections.

Post–Mortem Lesions

Placentitis is the most characteristic sign in ruminants. The placenta is typically leathery and thickened and may contain large quantities of white–yellow, creamy exudate at the edges of the cotyledons and in the intercotyledonary areas. In some cases, the exudate may be reddish– brown and fluid. Severe vasculitis is uncommon, but thrombi and some degree of vascular inflammation may be noted. Fetal pneumonia has been seen in goats and cattle and may occur in sheep; however, the lesions in aborted fetuses are usually non–specific.

Internet Resources

Animal Health Australia.
The National Animal Health Information System (NAHIS)
http://www.brs.gov.au/usr–bin/aphb/ahsq?dislist=alpha

Material Safety Data Sheets –Canadian Laboratory Center for Disease Control http://www.hc–sc.gc.ca/pphb–dgspsp/msds–ftss/index.html#menu

Medical Microbiology
http://www.gsbs.utmb.edu/microbook

Office International des Epizooties (OIE)

Manual of Standards for Diagnostic Tests and Vaccines
http://www.oie.int/eng/normes/mmanual/a_summry.htm

Q Fever: An Overview
United States Animal Health Association
http://www.usaha.org/speeches/speech01/s01conch.html

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http://www.merck.com/pubs/mmanual/

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Tularemia

rabbit fever, deerfly fever, Ohara's disease, Francis disease

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Etiology

Tularemia results from infection by *Francisella tularensis* (formerly known as *Pasteurella tularensis*), a Gram negative, non–motile coccobacillus. Two subspecies exist: *F. tularensis tularensis* (also known as Jellison type A) and *F. tularensis holarctica* (Jellison type B). *F. tularensis tularensis* is found in lagomorphs in North America and is highly virulent for humans and domestic rabbits; *F. tularensis* holarctica is less virulent and occurs in beaver, muskrats and voles in North America and in hares and small rodents in Eurasia.

Geographic Distribution

Tularemia occurs in North America, continental Europe, Russia, China and Japan. The subspecies *F. tularensis tularensis* is found in North America; *F. tularensis holarctica* is seen in North America and Eurasia.

Transmission

F. tularensis can be transmitted by ingestion, inhalation, arthropod–borne transfer or direct contact through the skin and mucous membranes. Organisms are found in the blood and tissues of infected animals and can survive for long periods on fomites including food and water. Aquatic animals may develop tularemia after being immersed in contaminated water. Carnivores sometimes become infected after ingesting a contaminated carcass. Vectors for *F. tularensis tularensis* include ticks (including *Dermacentor andersoni*, *D. variabilis* and *Amblyomma americanum*) and biting flies (particularly deerflies). *F. tularensis holarctica* is also transmitted by mosquitoes in Russia. Rarely, the organism is spread by animal bites.

F. tularensis can survive for long periods of time in arthropod vectors and in the environment. Individual flies may carry the organism for 2 weeks and ticks throughout their lifetimes. Viable bacteria can also be found for weeks to months in the carcasses and hides of infected animals and in fomites including grain dust, straw, water, soil and bedbugs. This organism is highly resistant to freezing; live organisms have been found after 3 years in rabbit meat stored at –15° C. *F. tularensis* has been weaponized.

Disinfection

F. tularensis is easily killed by disinfectants including 1% hypochlorite, 70% ethanol, glutaraldehyde and formaldehyde. It can also be inactivated by moist heat (121° C for at least 15 min) and dry heat (160–170° C for at least 1 hour). This bacterium remains viable at freezing temperatures for months to years.

Infections in Humans

Incubation Period

The incubation period in humans is 3 to 15 days; clinical signs usually appear after 3 to 5 days.

Clinical Signs

Six forms of tularemia are seen in humans: typhoidal, ulceroglandular, glandular, oculoglandular, oropharyngeal and pneumonic. The form of the disease depends on the inoculation site.

Typhoidal tularemia usually occurs after inhalation but can also develop after skin inoculation or ingestion. The clinical signs may include fever, prostration, headache, nausea and weight loss. Some patients become extremely weak and develop recurring chills and drenching sweats. A nonspecific rash may be seen but lymphadenopathy is usually absent. Pneumonia is particularly common in the typhoidal form and can be severe.

Ulceroglandular tularemia usually occurs after infection through the skin or mucous membranes. The clinical signs may include fever, chills, headache and malaise. The regional lymph nodes are typically enlarged and painful; they may suppurate and drain profusely. An inflamed papule usually develops where the initial

transmission occurred; it quickly turns into a pustule then ulcerates. On the extremities, single ulcers with thin, colorless, scanty exudates are usual. Glandular tularemia is characterized by fever and tender lymphadenopathy without a skin ulcer. Infection of the conjunctiva results in oculoglandular tularemia; this form is characterized by painful, unilateral, purulent conjunctivitis with preauricular or cervical lymphadenopathy. In some cases, there may be chemosis, periorbital edema and multiple small nodules or ulcerations on the conjunctiva. When the ulceroglandular disease occurs only in the throat, it is called oropharyngeal tularemia. In this form, there is an acute exudative or membranous pharyngotonsillitis with cervical lymphadenopathy.

Pneumonic tularemia can occur after inhalation or by secondary hematogenous spread. Victims develop severe, sometimes fulminant, atypical pneumonia. There may be signs of lung consolidation and, in come cases, delirium. Sometimes, the only symptoms may be a dry, unproductive cough, with decreased breath sounds and substernal discomfort. The pneumonic form can occur with any other form and has a high mortality rate. It develops in 10 to 15% of all cases of ulceroglandular tularemia and about 50% of cases of typhoidal tularemia.

Communicability

Person to person transmission has not been seen; however, infectious organisms can be found in the blood and other tissues.

Diagnostic Tests

Tularemia is often diagnosed by immunofluorescent staining of *F. tularensis* antigens in tissue samples or blood, and by serology. Commonly used serologic tests include tube agglutination, microagglutination and enzyme–linked immunosorbent assays (ELISA). A rising titer is diagnostic. Significant titers begin to appear during the second week of infection, although some specific antibodies are seen within the first 7 days. Cross–reactions occur with Brucella species, Proteus OX19, and Yersinia.

Tularemia can also be diagnosed by isolating *F. tularensis* from blood, sputum, pharyngeal or conjunctival exudates, ulcers, lymph nodes and gastric washings. *F. tularensis* does not grow well on standard media but may be isolated on media containing cysteine or sulfhydryl compounds. On McCoy medium, colonies are small, prominent, round and transparent. Confluent, milky, mucoid colonies develop on Francis medium and modified Thayer/Martin agar. Growth is slow and may take up to 3 weeks. Identification is by the absence of growth on ordinary media, morphology, immunofluorescence and slide agglutination. Organisms are non–motile, Gram negative small coccobacilli, with bipolar staining in young cultures. Bacteria from older cultures may be pleomorphic. *F. tularensis tularensis* can be distinguished from *F. tularensis* palaearctica by glycerol fermentation, ri*bos*omal RNA probes and polymerase chain reaction (PCR) tests. Organisms in culture are highly infectious to humans and special precautions must be taken during isolation.

Treatment and Vaccination

F. tularensis is susceptible to a variety of antibiotics. Relapses are not common but can occur if treatment is stopped before all bacteria are eliminated. Live attenuated vaccines may be recommended for people at a high risk of infection, such as laboratory workers.

Morbidity and Mortality

Tularemia can affect all ages. Infections occur most often in hunters, butchers, farmers, fur handlers and laboratory workers. In natural infections, ulceroglandular tularemia is the most common form; it occurs in 75 to 85% of cases. The typhoidal form is seen in 5 to 15%, the glandular form in 5–10% and the oculoglandular form in 1 to 2%. Typhoidal tularemia would be expected to be the predominant form after an attack by aerosolized *F. tularensis* in a biological weapon.

The mortality rate is approximately 30 to 35% for untreated *F. tularensis tularensis* infections and 5 to 15% for *F. tularensis holarctica* infections. Typhoidal tularemia is the most dangerous form; if untreated, the case fatality rate is approximately 35%. In contrast, the case fatality rate for the untreated ulceroglandular form is 5%. Naturally acquired cases are rarely fatal if treated; case fatality rates up to 1–3% are cited by some authorities. Higher fatality rates would be expected after a biological attack. Permanent immunity usually develops after a single episode of tularemia.

Infections in Animals

Species Affected

More than a hundred species of animals can be infected with F. tularensis. The natural hosts include cottontail and jack rabbits, hares, voles, vole rats, squirrels, muskrat, beaver and lemmings. Among domestic animals, sheep seem to be particularly susceptible to clinical disease. Tularemia has also been seen in dogs, cats, pigs and horses; cattle seem to be resistant. Infections in birds, reptiles and fish have been reported.

Incubation Period

The incubation period is 1 to 10 days.

Clinical Signs

The full spectrum of clinical signs is not known in animals. Many cases may be asymptomatic. Signs of septicemia can be seen in sheep and other mammals; symptoms may include fever, lethargy, anorexia, stiffness, increased pulse and respiration, coughing, diarrhea and pollakiuria. Rabbits and rodents may be depressed,

anorectic and ataxic, with a roughened coat and tendency to huddle. Anorexia, weight loss and vomiting have been reported in cats. Skin lesions are rarely seen in animals. Symptoms usually last 2 to 10 days in susceptible animals and may end in prostration and death. Susceptible species may be found dead without other symptoms.

Communicability

Yes. Infectious organisms can be found in the blood, tissues and feces. Humans and other animals can be infected through the skin or mucous membranes; routes of transmission include aerosols and ingestion. Infected cats may be able to transmit the organism in bites.

Diagnostic Tests

Impression smears of liver, spleen, bone marrow, kidney, lung or blood may be helpful for a presumptive diagnosis; small Gram negative coccobacilli can sometimes be found inside cells and scattered among tissue debris. *F. tularensis* is very small (0.2–0.7 µm) and easy to miss. Definitive diagnosis is by immunofluorescent detection of organisms in impression smears from these tissues, agglutination with specific antiserum, culture and occasionally serology. Animal inoculation can be used but it is dangerous and not recommended for routine identification.

F. tularensis can be isolated from enlarged lymph nodes, blood and tissues including liver, spleen and bone marrow; overgrowth of other bacteria may prevent recovery from animals found dead. This organism does not grow well on standard media but can be isolated on media containing cysteine or sulfhydryl compounds. On McCoy medium, colonies are small, prominent, round and transparent. Confluent, milky, mucoid colonies develop on Francis medium and modified Thayer/Martin agar. Growth is slow and may take up to 3 weeks. Identification is by the absence of growth on ordinary media, morphology, immunofluorescence and slide agglutination. The organisms are non–motile, Gram negative, small coccobacilli, with bipolar staining in young cultures. Bacteria from older cultures may be pleomorphic. *F. tularensis tularensis* can be distinguished from *F. tularensis holarctica* by glycerol fermentation, ri*bos*omal RNA probes and polymerase chain reaction (PCR) tests. Organisms in culture are highly infectious to humans and special precautions must be taken during isolation.

Serology is occasionally useful. Species sensitive to tularemia typically die before specific antibodies develop; however, significant titers can be found in more resistant species such as sheep, cattle, pigs, moose, dogs and birds. Available tests include tube agglutination and enzyme–linked immunosorbent assay (ELISA).

Treatment and Vaccination

Tularemia can be treated with various antibiotics but long–term treatment may be necessary; early treatment is expected to reduce mortality. Vaccines are not marketed specifically for animals.

Morbidity and Mortality

Tularemia is relatively common and often fatal in wild animals; disease is particularly common among rabbits, rodents, pheasants and quail. This disease is rare among domestic rabbits and rodents, but may be seen in animals kept outside. Outbreaks of *F. tularensis tularensis* infections, characterized by high mortality, have been seen in sheep. Mortality rates up to 15% are seen in untreated lambs.

Post–Mortem Lesions

Most animals with acute tularemia are in good body condition. The most consistent lesions are miliary, grayish–white necrotic foci in the liver and sometimes the spleen, bone marrow and lymph nodes. Some of these necrotic foci may be barely visible. Enlargement of the liver, spleen and lymph nodes is also common. In rabbits, the white necrotic foci on a dark, congested liver and spleen have been compared to the Milky Way. Congestion and edema is frequent in the lungs; consolidation and fibrinous pneumonia or pleuritis may also be found. The abdominal cavity sometimes contains fibrin. In some species, the lesions can resemble tuberculosis and chronic granulomas may be found in the liver, spleen, kidneys and lungs.

Internet Resources

Centers for Disease Control and Prevention (CDC) Tularemia Pages

http://www.bt.cdc.gov/agent/tularemia/index.asp

Material Safety Data Sheets–Canadian Laboratory Center for Disease Control
http://www.hc–sc.gc.ca/pphb–dgspsp/msds–ftss/index.html#menu

Medical Microbiology

http://www.gsbs.utmb.edu/microbook

The Merck Manual

http://www.merck.com/pubs/mmanual/

The Merck Veterinary Manual

http://www.merckvetmanual.com/mvm/index.jsp

USAMRIID's Medical Management of Biological Casualties Handbook

http://www.vnh.org/BIOCASU/toc.html

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Viral Hemorrhagic Fevers–Ebola and Marburg

African Hemorrhagic Fever

Last Updated: Apr. 2005

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Etiology

Ebola and Marburg are caused by Ebola virus and Marburg virus, the only members of the family Filoviridae. These two viruses are closely related and are considered to be serotypes or genotypes within a single genus. Ebola virus is subdivided into four subtypes: Zaire, Sudan, Reston, and Côte d'Ivoire.

Geographic Distribution

Ebola-Zaire, Ebola-Sudan, and Ebola-Côte d'Ivoire outbreaks have been seen in Sudan, Zaire, the Ivory Coast and the Democratic Republic of the Congo. Ebola-Reston outbreaks have occurred in non-human primates in the Italy and United States; these outbreaks were traced to monkeys imported from the Philippines. Wild non-human primates in the Philippines may have antibodies to Ebola-Reston.

Marburg has been seen in Angola, Uganda, Kenya, Zimbabwe and South Africa. Outbreaks also occurred in Germany and former Yugoslavia, in humans exposed to African green monkeys from East Africa.

Transmission

Human filovirus outbreaks seem to have a zoonotic source, but the reservoir host has not been identified although bats have been implicated in Marburg. Transmission among humans and other primates is by direct contact with infected blood, secretions, organs or semen, and on fomites. Virus has also been found in urine. Marburg and Ebola can be transmitted by aerosols and small droplets among monkeys; however, aerosol transmission does not appear to be a major route of spread between humans infected with Ebola. Filoviruses can survive for several weeks in blood and corpses.

Disinfection

Hypochlorite or phenolic disinfectants are generally recommended for disinfection. Ebola virus is susceptible to 2% sodium hypochlorite, 2% glutaraldehyde, 5% peracetic acid and 1% formalin. This virus is also inactivated by ultraviolet light, gamma irradiation, 0.3% betapropiolactone for 30 minutes at 37° C, or heating to 60° C for 1hr. Marburg virus is susceptible to 1% sodium hypochlorite, 2% glutaraldehyde or formaldehyde, ultraviolet light or heat.

Infections in Humans

Incubation Period

The incubation period is 2 to 21 days for Ebola and 3 to 10 days for Marburg.

Clinical Signs

Ebola usually begins with the abrupt onset of headache, sore throat, fever, myalgia, joint pain and weakness, followed by diarrhea, vomiting and stomach pain. A maculopapular rash on the truck, red eyes and hiccups are also seen. Hemorrhages are common and may include petechiae, ecchymoses, bloody diarrhea, bleeding from puncture sites and mucous membranes, and other internal and external bleeding. Early symptoms may be nonspecific and resemble other illnesses. Ebola-Reston can infect humans but hemorrhagic illnesses have not been seen.

The symptoms of Marburg are very similar to Ebola. This disease also begins with the acute onset of fever, chills, headache and myalgia. Approximately five days later, a maculopapular rash may appear on the trunk, followed by a sore throat, nausea, vomiting, chest pain, abdominal pain or diarrhea. Other symptoms may include severe weight loss, jaundice, delirium, shock, pancreatitis, liver failure, massive hemorrhaging and multi-organ dysfunction.

Communicability

Filoviruses can be spread between humans by contact with blood, secretions, organs, or semen. Ebola virus has been found in large quantities in the skin. Aerosol transmission is at least theoretically possible.

Viral Hemorrhagic Fevers–Ebola and Marburg

Diagnostic Tests

Early in the course of infection, Ebola can be diagnosed by an antigen-capture enzyme-linked immunosorbent assay (ELISA), virus isolation, detection of viral RNA by polymerase chain reaction (PCR) or the detection of virus-specific IgM by ELISA. Serology for IgG antibodies is useful later in the disease. At necropsy, immunohistochemistry, virus isolation or PCR can be employed.

Early Marburg infections can de diagnosed by antigen-capture ELISA, virus isolation, polymerase chain reaction (PCR) or an ELISA to detect Ebola-specific IgM. An IgG specific ELISA is useful later in the disease or after recovery. Diagnosis at necropsy is by immunohistochemistry on blood or tissue, virus isolation or PCR.

Treatment and Vaccination

No specific treatment is available for Ebola or Marburg; supportive therapy is given, with appropriate barrier precautions against infection of medical personnel. Transfusions of fresh-frozen plasma and other replacements for clotting proteins have been tried. Heparin has also been used, although its use is controversial.

Morbidity and Mortality

The case fatality rate is 50 to 90% for Ebola and 23 to 90% for Marburg. Bleeding is a poor prognostic sign. Ebola-Reston can infect humans but hemorrhagic illnesses have not been seen.

Infections in Animals

Species Affected

Ebola-Zaire, Ebola-Sudan and Ebola-Côte d'Ivoire affect humans and non-human primates; Ebola-Reston causes hemorrhagic fever in monkeys but does not seem to be pathogenic for humans. Naturally-occurring Ebola antibodies have been found in rhesus monkeys, African green monkeys, cynomolgus monkeys and baboons. Chimpanzees, gorillas, rhesus monkeys, vervet monkeys, cynomolgus monkeys, newborn mice and guinea pigs can develop clinical illness. Experimentally infected rabbits, pigeons and various species of mice, bats, frogs, geckos, snakes, tortoises and arthropods did not develop clinical signs; however, virus replication was seen in bats and possibly snakes, mice and spiders. The natural reservoir of this virus is unknown.

Marburg virus can infect humans and non-human primates, including African green monkeys. Antibodies have been found in captive vervet monkeys and baboons in Kenya. The natural host is unknown but bats have been implicated.

Incubation Period

The incubation period for Marburg or Ebola-Zaire infections in rhesus monkeys and African green monkeys is 4 to 16 days. In guinea pigs, the incubation period is 4 to 10 days.

Clinical Signs

Filovirus infections result in severe, often fatal, hemorrhagic fevers in non-human primates. Clinical signs may include fever, anorexia, vomiting, splenomegaly, weight loss and a skin rash. Hemorrhages can occur in any organ and may include petechiae, bleeding into the gastrointestinal tract, or bleeding from puncture wounds and mucous membranes. Guinea pigs infected with unpassaged virus from primates usually develop a fever and weight loss but recover; animals infected with serially passaged virus may develop fatal liver disease.

Communicability

Blood, secretions, organs, semen and urine may contain infectious virus; virus can probably be found almost anywhere in the body. Aerosol transmission of both Ebola and Marburg viruses has been seen in primates.

Diagnostic Tests

Filovirus infections can be diagnosed by virus isolation; Vero cells or MA-104 cells are commonly used for Ebola virus. In humans, Ebola virus is most reliably isolated from acute-phase serum but can also be found in throat washes, urine, semen, anterior eye fluid and other fluids. In necropsied monkeys, filoviruses have been found in particularly high concentrations in the liver, spleen, lungs and lymph nodes. Electron microscopy can also detect virus particles in tissues: filoviruses are pleomorphic, long and filamentous and may be branched. Some may be U-shaped, b-shaped or circular. Viral antigens can be detected with an enzyme-linked immunosorbent assay (ELISA) or by immunofluorescence. Skin biopsies collected into formalin may be helpful for diagnosis; large amounts of Ebola antigen have been found in skin. A reverse transcriptase-polymerase chain reaction (RT-PCR) assay can identify Marburg or Ebola RNA.

Serologic tests include indirect immunofluorescence assays (IFA), immunoblotting and ELISAs. Neutralization tests are unreliable for filoviruses. Paired serum samples should be tested; low IFA titers in single samples cannot be interpreted. The significance of antibody titers in asymptomatic primates is controversial.

Treatment and Vaccination

No specific therapy or vaccine is available.

Morbidity and Mortality

Marburg and Ebola infections have a very high mortality rate in non-human primates and experimentally infected suckling mice. Guinea pigs infected with Ebola

virus from primates usually recover; animals infected with serially passaged virus may develop fatal liver disease.

Post-Mortem Lesions

At necropsy, there may be widespread petechiae and hemorrhages. Hemorrhages can occur in any organ but are particularly common in the gastrointestinal tract, kidneys, and pleural, pericardial and peritoneal spaces. The liver and spleen may be swollen and friable. Animals may have a maculopapular rash. There can also be signs of interstitial pneumonia, nephritis, and necrosis of the liver, lymphoid tissue, adrenal cortex or pulmonary epithelium.

Internet Resources

Centers for Disease Control and Prevention (CDC) –Viral Hemorrhagic Fevers Index

http://www.bt.cdc.gov/agent/vhf/index.asptm

"Marburg and Ebola Viruses" in Encyclopedia of Virology

http://www.bocklabs.wisc.edu/eov-ebola.html

Material Safety Data Sheets– Canadian Laboratory Center for Disease Control http://www.hc-sc.gc.ca/pphb-dgspsp/msds-ftss/index.html#menu

Medical Microbiology

http://www.gsbs.utmb.edu/microbook

Pathology of Nonhuman Primates from Primate Info Net. Wisconsin Primate Research Center

http://www.primate.wisc.edu/pin/pola6-99.html

Primate Info Net. Wisconsin Primate Research Center

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USAMRIID's Medical Management of Biological Casualties Handbook

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Section 2

High-Consequence Livestock Pathogens

African Swine Fever

Pesti Porcine Africaine, Peste Porcina Africana, Maladie de Montgomery

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Importance

African swine fever is a serious viral disease of pigs, endemic in Africa. Isolates vary in virulence from highly pathogenic strains that cause near 100% mortality to low–virulence isolates that can be difficult to diagnose. Disease outbreaks have occurred in numerous countries and the cost of eradication has been significant. During outbreaks in Malta and the Dominican Republic, the swine herds of these countries were completely depopulated.

Etiology

African swine fever results from infection by the African swine fever virus (ASFV). Formerly classified as a member of the Iridoviridae, this virus is currently the only member of a family called "Asfarviridae." The ASF virus is the only DNA virus that is transmitted by arthropods. The virulence of virus isolates varies.

Species affected

African swine fever affects domestic pigs and wild pigs, including the warthog, bush pig, and giant forest hog in Africa and the feral pig in the island of Sardinia, Italy. Symptomatic infections occur in domestic pigs and feral pigs; infections are generally asymptomatic in warthogs, bush pigs, and giant forest hogs.

Geographic distribution

African swine fever is endemic in most of sub–Saharan Africa; the highest incidence of disease is seen from the Equator to the northern Transvaal. This disease is also found in feral pigs in Sardinia, Italy.

Transmission

African swine fever can be transmitted by direct contact with infected animals, indirect contact on fomites, and by tick vectors. Transmission during direct contact is usually by oronasal spread. African swine fever virus can be found in all tissues and body fluids, but particularly high levels are found in the blood. Massive environmental contamination may result if blood is shed during necropsies or pig fights, or if a pig develops bloody diarrhea. The virus can also spread on fomites, including vehicles, feed, and equipment. There is evidence that some pigs may become carriers.

African swine fever often spreads to new areas when pigs are fed uncooked scraps that contain ASFV–infected pork. In one outbreak, pigs became infected after being fed the intestines of guinea fowl that had eaten infected ticks. The African swine fever virus is highly resistant to environmental conditions. It can survive for 15 weeks in chilled meat, a year and a half in blood stored at 4º C, 11 days in feces at room temperature, and at least a month in contaminated pig pens. The virus will also remain infectious for 150 days in boned meat stored at 39º F, 140 days in salted dried hams, and several years in frozen carcasses.

African swine fever is also spread through the bite of infected soft ticks *Ornithodoros spp*.ticks. In tick populations, transstadial, transovarial, and sexual transmission occur. In Africa, this disease is thought to cycle between newborn warthogs and the soft ticks that live in their burrows. Infected soft tick colonies can maintain the ASF virus for long periods of time, measured in years.

Incubation period

The incubation period is 5 to 15 days.

Clinical signs

African swine fever can be a peracute, acute, subacute, or chronic disease. More virulent isolates cause a high fever, moderate anorexia, leukopenia, recumbency, and skin reddening that is most apparent in white pigs. Some pigs develop cyanotic skin blotching on the ears, tail, lower legs, or hams. Diarrhea and abortions are sometimes seen, but most pigs infected with this virus remain in good condition. In infections with highly virulent isolates, progressive anorexia and depression develop and are usually followed by death within 7 to 10 days. The death rate is generally lower in ani-

mals infected with moderately virulent isolates, but may still be very high in very young animals.

Animals infected with isolates of low virulence may seroconvert without symptoms, abort, or develop chronic African swine fever. The symptoms of chronic disease are a low fever, which may recur, and sometimes pneumonia or painless swelling of the joints, particularly the carpal and tarsal joints. Reddened foci may appear on the skin and become raised and necrotic. In some cases, the only clinical signs may be emaciation and stunting. Chronic African swine fever can be fatal.

Post mortem lesions

The most consistent and characteristic lesions occur in the spleen and lymph nodes. In animals infected with highly virulent isolates, the spleen is usually very large, friable, and dark red to black. In pigs infected with moderately virulent isolates, the spleen is also enlarged, but not friable, and the color is closer to normal. The lymph nodes are often swollen and hemorrhagic and may look like blood clots; the nodes most often affected are the gastrohepatic, renal, and mesenteric lymph nodes. Edema may also be seen in other lymph nodes, and the tonsils are often swollen and reddened.

Less consistent clinical signs include hemorrhages, petechiae, and ecchymoses in other organs. Petechiae may be present on any organ, but most are located on the renal cortex, bladder, lungs, and heart. Ecchymoses and "paint–brush" hemorrhages are often found on the serosa of the stomach and intestines. Edema may be seen in the lungs and gall bladder, and the pleural, pericardial, and peritoneal cavities may contain excess fluid. In some pigs, dark red or purple areas may be found on the skin of the ears, feet, and tail. Aborted fetuses may be anasarcous, have a mottled liver, and contain petechiae in the placenta, skin, and myocardium.

In animals with chronic African swine fever, the most common post–mortem lesions are focal areas of skin necrosis, consolidated lobules in the lung, fibrinous pericarditis, generalized lymphadenopathy, and swollen joints.

Morbidity and Mortality

In domestic pigs, morbidity approaches 100% in herds that have not been previously exposed to the virus. Mortality varies with the virulence of the isolate, and can range from 0% to 100%. Low virulence isolates are more likely to be fatal in pigs with a concurrent disease, pregnant animals, and young animals. Mild or asymptomatic disease is usually seen in warthogs and bush pigs.

No treatment or vaccine exists for this disease.

Diagnosis

Clinical

African swine fever should be suspected in pigs with a fever, when the necropsy findings include a very large, friable, dark red to black spleen and greatly enlarged and hemorrhagic gastrohepatic and renal lymph nodes.

Differential diagnosis

The differential diagnosis includes hog cholera (classical swine fever), porcine dermatitis and nephropathy syndrome, erysipelas, salmonellosis, eperythrozoonosis, actinobacillosis, Glasser's disease (*Haemophilus parasuis* infection), Aujeszky's disease, thrombocytopenic purpura, warfarin poisoning, and heavy metal toxicity.

Laboratory tests

In areas where African swine fever is not endemic, this disease should be diagnosed by virus isolation and the detection of viral antigens. Blood and tissue samples from suspect pigs are inoculated into pig leukocyte or bone marrow cultures for virus isolation. African swine fever virus induces hemadsorption of pig erythrocytes to the surface of infected cells. The virus can also be detected with peripheral blood leukocytes from infected pigs in a hemadsorption "autorosette" test.

African swine fever virus antigens can be found in tissue smears or cryostat sections by the fluorescent antibody test (FAT). Nucleic acids can be detected by a polymerase chain reaction (PCR) assay. PCR is particularly useful in putrefied samples that cannot be used for virus isolation and antigen detection.

Serology is carried out simultaneously with virus isolation. Antibodies to ASFV persist for long periods of time after infection. Serology may also be used for diagnosis in endemic areas. Available serologic tests include the enzyme–linked immunosorbent assay (ELISA), immunoblotting, indirect fluorescent antibody (IFA), and counter immunoelectrophoresis (immunoelectro–osmophoresis) tests. The ELISA is prescribed for international trade.

Samples to collect

Before collecting or sending any samples from animals with a suspected foreign animal disease, the proper authorities should be contacted. Samples should only be sent under secure conditions and to authorized laboratories to prevent the spread of the disease.

For virus isolation from live animals, blood should be collected into an anticoagulant and antibiotics should be added. At necropsy, samples of the spleen, lung, liver, kidney, and tonsils, as well as the submandibular, inguinal, and gastrohepatic lymph nodes should be collected aseptically. Samples of the bone marrow should be sent if significant postmortem changes are seen. ASFV is not

found in aborted fetuses; in cases of abortion, a blood sample should be collected from the dam. Samples for virus isolation should be transported cold on wet ice or frozen gel packs.

Samples of the same tissues, the brain, and any other grossly abnormal tissues should be submitted for histology. Serum and/ or tissue fluids should be submitted for serology

Recommended actions if African swine fever is suspected

Notification of authorities

African swine fever should be reported to state or federal authorities immediately upon diagnosis or suspicion of the disease. Federal: Area Veterinarians in Charge (AVICS) http://www.aphis.usda.gov/vs/area_offices.htm

State vets: http://www.aphis.usda.gov/vs/sregs/official.html

Quarantine and Disinfection

To prevent introduction of the African swine fever virus into areas free of the disease, all garbage fed to pigs should be cooked. Unprocessed meat must be heated to at least 70ºC for 30 minutes to inactivate the virus; 30 minutes at 60ºC is sufficient for serum and bodily fluids.

African swine fever is a contagious disease. Eradication is by slaughter of infected and in–contact animals, and disposal of carcasses, often by burying, rendering or burning. Strict quarantine must be imposed, and potential tick vectors should be controlled with acaricides. In cases of ASF outbreaks, there must be a detailed entomological investigation for the possibility of soft tick vectors and their role as long term carriers. In the outbreaks in the Americas, the Ornithodoros ticks never became chronically infected. But in Spain, Portugal and Africa, infected soft ticks can carry the ASFV for many years. Many common disinfectants are ineffective; care should be taken to use a disinfectant specifically approved for African swine fever. Sodium hypochlorite and some iodine and quaternary ammonium compounds are effective.

Public health

Humans are not susceptible to African swine fever virus.

For More Information

World Organization for Animal Health (OIE)

http://www.oie.int

OIE Manual of Standards

http://www.oie.int/eng/normes/mmanual/a_summry.htm

OIE International Animal Health Code

http://www.oie.int/eng/normes/mcode/A_summry.htm

USAHA Foreign Animal Diseases book

http://www.vet.uga.edu/vpp/gray_book/FAD/

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Classical Swine Fever

Hog Cholera, Peste du Porc, Colera Porcina, Virusschweinepest

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Importance

Classical swine fever is a serious and highly contagious viral disease of pigs. Acute or chronic infections occur; both are usually fatal. In herds infected with less virulent isolates, the only symptom may be poor reproductive performance or a failure to thrive. A wide range of clinical signs and a similarity to other diseases can make classical swine fever challenging to diagnose.

Etiology

Classical swine fever results from infection by classical swine fever virus (CSFV), (genus Pestivirus, family Flaviviridae). This virus is also known as hog cholera virus. Only one serotype has been found. The CSF virus is very similar to the Bovine Virus Diarrhea (BVD) virus that affects cattle.

Species affected

Classical swine fever affects domestic and wild pigs.

Geographic distribution

Classical swine fever is found in East and Southeast Asia, the Indian subcontinent, China, East and Central Africa, and most of South and Central America. This disease has been eradicated from the United States, Canada, New Zealand, and Australia. Most of Western Europe is free of classical swine fever; however, foci of infection remain in Germany and some countries of Eastern Europe.

Transmission

Classical swine fever is highly contagious. Virus transmission is mainly oral; CSFV is often spread by feeding uncooked contaminated garbage. Animals can also be infected through the mucus membranes, conjunctiva, and skin abrasions. Aerosol spread is sometimes seen in confined spaces; however, the virus does not travel long distances in the air. Infected carrier sows may give birth to persistently infected pigs. Mechanical spread by fomites and insects occurs.

Infected pigs are the only reservoir of virus. Blood, secretions and excretions, and tissues contain infectious virus. CSFV is moderately fragile in the environment, but can remain infectious for months in refrigerated meat and years in frozen meat. It can survive in contaminated pens and on fomites for as long as two weeks.

Incubation period

Variable incubation periods have been published, ranging from 2 to 14 days.

Clinical signs

The clinical signs of classical swine fever vary with the strain of virus and susceptibility of the pigs. More virulent strains cause acute disease; less virulent strains can result in a high percentage of chronic, mild, or asymptomatic infections.

In acute classical swine fever, common clinical signs include a high fever, dullness, weakness, drowsiness, huddling, anorexia, an unsteady gait, conjunctivitis, and constipation followed by diarrhea. Several days after the first symptoms appear, the abdomen, inner thighs, and ears may develop a purple discoloration. Convulsions may be seen in the terminal stages. Pigs with acute classical swine fever often die within one to two weeks.

The symptoms of chronic disease include intermittent fever, anorexia, periods of constipation or diarrhea, stunted growth, and alopecia. Immunosuppression may lead to concurrent infections. The symptoms of chronic infections can wax and wane for weeks to months and may affect only a few animals in the herd. Chronic infections are almost always fatal.

Reproductive symptoms may also be seen. Virulent strains can cause abortions or the death of piglets soon after birth. Less virulent strains of CSFV may result in stillbirths or mummification. Some piglets are born with a congenital tremor or congenital malformations of the visceral organs and central nervous system. Other piglets are asymptomatic but persistently infected. These animals are persistently viremic and

become clinically ill after several months. They may have mild anorexia, depression, stunted growth, dermatitis, diarrhea, conjunctivitis, ataxia, or paresis, and may die. In some breeding herds infected by less virulent strains, poor reproductive performance is the only sign of disease.

Post mortem lesions

The lesions of classical swine fever are highly variable. In acute disease, the most common lesion is hemorrhage. The skin may be discolored purple and the lymph nodes may be swollen and hemorrhagic. Petechial or ecchymotic hemorrhages can often be seen on serosal and mucosal surfaces, particularly the kidney, urinary bladder, epicardium, larynx, trachea, intestines, subcutaneous tissues, and spleen. Straw–colored fluid may be found in the peritoneal and thoracic cavities and the pericardial sac. Necrotic foci are common in the tonsils. Splenic infarcts are occasionally seen. The lungs may be congested and hemorrhagic. In some acute cases, lesions may be absent or inconspicuous.

The lesions of chronic disease are less severe and may be complicated by secondary infections. In addition, necrotic or "button" ulcers may be found in the intestinal mucosa, epiglottis and larynx.

In congenitally infected piglets, common lesions include cerebellar hypoplasia, thymic atrophy, ascites, and deformities of the head and legs.

Morbidity and Mortality

Both morbidity and mortality are high in acute infections. The mortality rate in acute cases can reach 90%. Chronic infections are also fatal in most cases.

Vaccines may be available in some areas. Vaccines can protect animals from clinical disease, but do not prevent infections. Good vaccination programs can eventually eliminate the infection in herds.

Diagnosis

Clinical

Classical swine fever should be suspected in pigs with septicemia and a high fever, particularly if uncooked scraps have been fed, unusual biological products have been used, or new animals have been added to the herd. Differentiation from other diseases may be difficult without laboratory testing. In acute outbreaks, the chance of observing the characteristic necropsy lesions is better if four or five pigs are examined.

Differential diagnosis

The differential diagnosis includes African swine fever, porcine dermatitis and nephropathy syndrome, erysipelas, eperythrozoonosis, salmonellosis, actinobacillosis, Glasser's disease (*Haemophilus suis* infection), thrombocytopenia purpura, warfarin poisoning, Aujeszky's disease, heavy metal poisoning, and salt poisoning. Pigs congenitally infected with bovine virus diarrhea (BVD) virus may look very similar to pigs with classical swine fever.

Laboratory tests

Classical swine fever can be diagnosed by detecting the virus or its antigens in whole blood or tissue samples. Virus antigens are detected by direct immunofluorescence or enzyme–linked immunosorbent assays (ELISAs). CSFV is differentiated from other pestiviruses by immunofluorescence testing with monoclonal antibodies. The virus can also be isolated in several cell lines including PK–15 cells; it is identified by direct immunofluorescence or peroxidase staining. Reverse transcriptase polymerase chain reaction (RT–PCR) tests are available.

Serology is used for diagnosis and surveillance. The most commonly used tests are virus neutralization tests, including the fluorescent antibody virus neutralization (FAVN) test, the neutralizing peroxidase–linked assay (NPLA), and ELISAs. Antibodies usually develop during the third week after infection, but cannot be reliably detected until 30 days after infection. They persist for life. Antibodies against ruminant pestiviruses may be found in breeding animals; only tests that use monoclonal antibodies can differentiate between these viruses and CSFV.

Samples to collect

Before collecting or sending any samples from animals with a suspected foreign animal disease, the proper authorities should be contacted. Samples should only be sent under secure conditions and to authorized laboratories to prevent the spread of the disease.

Samples should be taken from at least four pigs. In live pigs, whole blood is preferred but tonsil biopsies are sometimes useful. Serum samples should be taken from recovered animals or sows that have been in contact with suspected cases.

At necropsy, the tonsils should be submitted for virus isolation or antigen detection. Other organs to collect include the submandibular and mesenteric lymph nodes, spleen, kidneys, and the distal part of the ileum. Samples for antigen detection and virus isolation should be refrigerated but not frozen; they should be kept cold during shipment to the laboratory. A complete set of tissues, including the whole brain, should be submitted in 10% buffered formalin for histology.

Recommended actions if classical swine fever is suspected

Notification of authorities

Classical swine fever should be reported immediately upon diagnosis or suspicion of the disease.

Federal: Area Veterinarians in Charge (AVICS) http://www.aphis.usda.gov/vs/area_offices.htm

State vets: http://www.aphis.usda.gov/vs/sregs/official.html

Quarantine and Disinfection

CSFV is moderately fragile in the environment. This virus is sensitive to drying and ultraviolet light and is rapidly inactivated by a pH less than 3. Sodium hypochlorite and phenolic compounds are effective disinfectants. CSFV can survive for long periods in meat, but is destroyed by cooking.

During outbreaks, confirmed cases and contact animals may be slaughtered and aquarantine imposed. Vaccination may be used as a tool to assist in controlling an outbreak and eradicating the disease. In countries free of classical swine fever, periodic serologic sampling is necessary to monitor for the potential reintroduction of disease.

Public health

Classical swine fever does not affect humans.

For More Information

World Organization for Animal Health (OIE)

http://www.oie.int

OIE Manual of Standards

http://www.oie.int/eng/normes/mmanual/a_summry.htm

OIE International Animal Health Code

http://www.oie.int/eng/normes/mcode/A_summry.htm

USAHA Foreign Animal Diseases book

http://www.vet.uga.edu/vpp/gray_book/FAD/

Animal Health Australia. The National Animal Health Information System (NAHIS)

http://www.aahc.com.au/nahis/disease/dislist.asp>

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Foot and Mouth Disease (FMD)

Fiebre Aftosa

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Importance

Foot-and-mouth disease (FMD) is highly contagious and can rapidly spread through a region if control and eradication practices are not put into place as soon as the disease is identified. Weight loss, poor growth, permanent hoof damage, and chronic mastitis are just some of the sequelae of infection. As a result, international trade embargoes could cause significant economic losses.

Etiology

The foot-and-mouth disease virus (FMDV) is in the family Picornaviridae, genus *Aphthovirus*. There are 7 immunologically distinct serotypes and over 60 subtypes. New subtypes occasionally develop spontaneously. The FMDV is inactivated at a pH below 6.5 or above 11. The virus can survive in milk and milk products when regular parteurization temperatures are used. However, it is inactivated when ultra high pasteurization procedures are used. Virus stability increases at lower temperatures. It can survive in frozen bone marrow or lymph glands. In organic material such as serum, the virus can survive drying. It can remain active for days to weeks on organic rich materials under moist and cool temperatures. It is inactivated on dry surfaces and by UV radiation (sun light)

Species affected

FMDV primarily affects cloven-hoofed domestic and wild animals, including cattle, pigs, sheep, goats, and water buffalo. Other susceptible species include hedgehogs, armadillos, nutrias, elephants, capybaras, rats, and mice.

Geographic distribution

Foot-and-mouth disease was found worldwide after World War II. The last U.S. outbreak was in 1929. Endemic areas are Asia, Africa, the Middle East, and parts of South America. Epidemics occurred in recent years in Taiwan, South Korea, Japan, Mongolia, Britain, France, and The Netherlands. North and Central America, Australia, and New Zealand have been free for many years.

Transmission

Transmission primarily occurs by respiratory aerosols and direct or indirect contact with infected animals. Aerosol transmission requires proper temperature and humidity. Aerosol spread has occurred from bulk milk trucks. After conditions of heavy aerosol inhalation, FMDV can survive for 24 hours in the human respiratory tract. Feeding of infected animal products such as meat, milk, bones, glands and cheese can also spread the disease. Contact with contaminated objects such as boots, hands or clothing can be a source of infection. Another source of infection is artificial insemination and contaminated biologicals and hormone preparations.

Sheep and goats are considered maintenance hosts. They can have very mild signs; therefore, diagnosis may be delayed allowing time for aerosol and contact spread and environmental contamination. In pigs, FMDV spreads rapidly due to thousands of times higher virus particle concentration in aerosols as compared with other species. They are considered amplifying hosts. Cattle are considered 'indicators' of this disease because they generally are the first species to show signs of infection. Their lesions are more severe and progress more rapidly.

Ruminants can carry the virus for long periods in their pharyngeal tissue. Recovered or vaccinated cattle exposed to diseased animals can be healthy carriers for 6-24 months. Sheep can be carriers for 4-6 months. Pigs are not carriers of FMDV. Some strains of the virus can affect one species more than others.

Incubation period

Animals in contact with clinically infected animals will generally develop signs of disease in 3-5 days. The virus can enter through damaged oral epithelium or the tonsils in pigs fed contaminated garbage. In this case signs can be seen in 1-3 days. Experimental exposure can elicit signs in 12-48 hours. Peak time of shedding of the virus and transmission usually occurs when vesicles rupture.

Foot and Mouth Disease (FMD)

Clinical signs

Foot-and-mouth disease is characterized by fever and vesicles (blisters), which progress to erosions in the mouth, nares, muzzle, feet, or teats. Typical clinical signs include depression, anorexia, excessive salivation, serous nasal discharge, decreased milk production, lameness, and reluctance to move. Abortion may occur in pregnant animals is due to high fever (FMD virus does not cross the placenta). Death in young animals is due to severe myocardial necrosis. In cattle, oral lesions are common with vesicles on the tongue, dental pad, gums, soft palate, nostrils, or muzzle. Hoof lesions are in the area of the coronary band and interdigital space. In pigs the hoof lesions are usually severe with vesicles on the coronary band, heel, and interdigital space. Vesicles can be seen on the snout. Oral lesions are not as common as in cattle and are usually less severe. Drooling in pigs is rare. Sheep and goats show very mild, if any, signs of fever, oral lesions, and lameness. Animals generally recover in about 2 weeks with very low mortality in adult animals. Secondary infections may lead to a longer recovery time.

Post mortem lesions

The diagnostic lesions of foot-and-mouth disease are single or multiple vesicles from 2mm to 10cm in size. Lesions may be seen in any stage of development from a small white area to a fluid filled blister, sometimes joining with adjacent lesions. The vesicles rupture, leaving a red eroded area, which is then covered with a gray fibrinous coating. This coating becomes yellow, brown, or green then is replaced by new epithelium with a line of demarcation that gradually fades. Occasionally the fluid may escape through the epidermis instead of forming a vesicle. These "dry" lesions appear necrotic instead of vesicular. "Dry" lesions are more common in the pig oral cavity. Lesions at the coronary band progress similarly: the skin and hoof separate and, as healing occurs, a line showing evidence of coronitis appears on the hoof. Pigs may actually lose the hoof in severe cases. "Tiger heart" lesions may also be seen; these lesions are characterized by a gray or yellow streaking in the myocardium caused by degeneration and necrosis. Vesicular lesions may also be seen on the rumen pillars.

Morbidity and Mortality

Morbidity can be 100% in a susceptible population. Mortality is generally less than 1%. In younger animals or with more severe strains mortality can increase.

Diagnosis

Clinical

Clinical signs of concurrent salivation and lameness with vesicular lesions should make foot-and-mouth disease a differential consideration. Fever is often the first sign, so these animals should be carefully examined for early lesions on the mouth and hooves. The mouth of any lame animal, and the feet of animals with oral lesions or drooling, should also be checked. Tranquilization may be necessary for a thorough examination as vesicles may be difficult to see. Laboratory testing is an absolute requirement to confirm FMDV infection as all vesicular diseases have almost identical clinical signs.

Differential diagnosis

The clinical signs of foot-and-mouth disease can be similar to vesicular stomatitis, swine vesicular disease, vesicular exanthema of swine, foot rot, and chemical and thermal burns. In cattle, oral lesions seen later in the progression of FMD can resemble rinderpest, infectious bovine rhinotracheitis (IBR), bovine virus diarrhea (BVD), malignant catarrhal fever (MCF), and bluetongue. In sheep, these later lesions can resemble bluetongue, contagious ecthyma, and lip and leg ulceration.

Laboratory tests

FMDV can be identified using enzyme-linked immunosorbent assay (ELISA), complement fixation, and virus isolation. Virus isolation is done by inoculation of primary bovine thyroid cells and primary pig, calf and lamb kidney cells, inoculation of BHK-21 and IB-RS-2 cell lines, or inoculation of mice. ELISA and virus neutralization tests can be used to detect antibodies in serum. Virus isolation and identification must be performed on the initial case. Subsequently, antigen or nucleic acid detection can be used to diagnose additional cases in an outbreak.

Samples to collect

Before collecting or sending any samples from vesicular disease suspects, the proper authorities should be contacted. Samples should only be sent under secure conditions and to authorized laboratories to prevent spread of the disease. Since vesicular diseases can not be distinguished clinically, and some are zoonotic, samples should be collected and handled with all appropriate precautions. Samples include vesicular fluid, the epithelium covering vesicles, esophageal-pharyngeal fluid, unclotted whole blood collected from febrile animals and fecal and serum samples from infected and non-infected animals.

Recommended actions if foot-and-mouth disease is suspected

Notification of authorities

A quick response is vitally important in containing an outbreak of foot-and-mouth disease. State and federal veterinarians should be immediately informed of any suspected vesicular disease. Federal: Area Veterinarians

in Charge (AVICS) http://www.aphis.usda.gov/vs/area_offices.htm

State vets: http://www.aphis.usda.gov/vs/sregs/official.html

Quarantine and Disinfection

Suspected animals should be quarantined immediately and the premises should be disinfected. Sodium hydroxide (2%), sodium carbonate (4%), and citric acid (0.2%) are effective disinfectants. Less ideal disinfectants include iodophores, quaternary ammonium compounds, hypochlorite, and phenols, because they rapidly lose the ability to disinfect in the presence of organic matter. There are newer disinfectants that are better than and not as corrosive as some of these listed, included a chlorinated compound, Vircon-S®.

Vaccination

FMD vaccines used as prophylactic in a particular area are of the world, or used for control of an outbreak, must closely match the type and subtype of the prevalent FMDV strain. With seven serotypes, and more than 60 subtypes of FMDV, this task is one of the biggest challenges in FMD vaccination. Currently, there is no universal vaccine against FMD. The U.S., Canada, and Mexico maintain the North American FMD Vaccine Bank which contains vaccine strains for the most prevalent circulating serotypes in the world. The decision to use vaccination in control and eradication efforts is complex and depends upon scientific, economic, political, and societal factors specific to the outbreak situation. The final decision to use vaccination as an aid in controlling an outbreak of FMD in the U.S., Canada, or Mexico would be made by the Chief Veterinary Officer in each country.

Public health

FMDV infections in humans are rare, with just over 40 cases diagnosed since 1921. Vesicular lesions can be seen, but the signs are generally mild. Foot-and-mouth disease is not considered to be a public health problem.

For More Information

World Organization for Animal Health (OIE)

http://www.oie.int

OIE Manual of Standards

http://www.oie.int/eng/normes/mmanual/a_summry.htm

OIE International Animal Health Code

http://www.oie.int/eng/normes/mcode/A_summry.htm

USAHA Foreign Animal Diseases book

http://www.vet.uga.edu/vpp/gray_book/FAD/

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Influenza

Flu, Grippe, Swine Influenza, Hog Flu, Pig Flu, Equine Influenza, Avian Influenza

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Etiology

Viruses in the family Orthomyxoviridae cause influenza. There are three genera of influenza viruses: influenzavirus A, influenzavirus B and influenzavirus C.[1] These viruses are also called type A, type B and type C. Type A viruses include the avian, swine and equine influenza viruses, as well as the human influenza A viruses. The influenza B and C viruses are mainly found in humans, although there is increasing evidence that they can also infect other species.

Influenza A viruses

Influenza A viruses are classified into subtypes based on two surface antigens, hemagglutinin (H) and neuraminidase (N).

There are 15 hemagglutinin antigens (H1 to H15) and 9 neuraminidase antigens (N1 to N9).[2-7] These two proteins are involved in cell attachment and release from cells, and are also major targets for the immune response.[8-11] Only limited subtypes are found in each species of mammal.[11]

Subtypes of influenza A viruses are classified into strains. Strains of influenza viruses are described by their type, host, place of first isolation, strain number (if any), year of isolation, and antigenic subtype.[11,12] [e.g., the prototype strain of the H7N7 subtype of equine influenza virus, first isolated in Czechoslovakia in 1956, is A/eq/Prague/56 (H7N7).] For human strains, the host is omitted.

Influenza A viruses change frequently. New strains and subtypes can cause epidemics and pandemics. Strains evolve as they accumulate point mutations during virus replication. (antigenic drift).[11] Genetic reassortment can occur if two different influenza viruses infect a cell simultaneously.[10] Reassortment between two different strains results in the periodic emergence of novel strains. Reassortment between subtypes can result in the emergence of a new subtype. Reassortment can occur between avian, swine, equine and human influenza A viruses. This type of reassortment can result in a 'hybrid' virus with, for example, both avian and human influenza virus proteins.

An abrupt change in the subtypes found in host species is called an 'antigenic shift.' Antigenic shifts can result from three mechanisms which include the direct transfer of a whole virus from one host species into another - e.g., an avian influenza virus spreading in pigs, reassortment between subtypes, or the re-emergence of a virus that was found previously but is no longer in circulation.[9,12] For example, human viruses can continue to circulate in pigs and could re-emerge into the human population.[9]

Avian influenza viruses

Avian influenza viruses are found in a wide variety of domestic and wild birds.[3,12,13] They are also isolated occasionally from mammals including humans.[3,5,7,9,12,15-17] Waterfowl, which seem to be the natural reservoirs for the type A influenza viruses, carry all of the known subtypes.[2,7,9,12-20] The predominant subtypes in wild ducks change periodically.[12] Poultry can be infected by a wide variety of subtypes. From 1993 to 2000, subtypes containing H1 to H7 and H9 to H11 were isolated from live bird markets in the northeastern U.S.[21]

Avian influenza viruses are classified as either highly pathogenic avian influenza (HPAI) or low pathogenic avian influenza (LPAI), based on the genetic features of the virus and the severity of disease in poultry.[2,3] To date, only subtypes that contained H5 or H7 have been highly pathogenic; subtypes that contained other hemagglutinins have been found only in the LPAI form.[6,20,22] H5 and H7 LPAI viruses also exist, and can evolve into highly pathogenic strains.[3,19,20] Subtypes found in ratites have included H3N2, H4N2, H4N6, H5N2, H5N9, H7N1, H7N3, H9N2, H10N4 and H10N7.[22] All were of low virulence for chickens. Isolates from cage birds usually contain H3 or H4.[22]

Swine influenza viruses

Swine influenza viruses are found mainly in pigs, but have also been found in other species including humans.[7,9,11,12,23,24] There is less antigenic drift in swine influenza A viruses than in human viruses.[9] The most common subtypes currently found in pigs are H1N1, H1N2 and H3N2.[25] Although the swine influenza viruses found in the U.S. and Europe are the same subtypes, they are actually different viruses.

The 'classical' H1N1 swine influenza virus, found in pigs since 1918, circulates in the U.S.[9,10,12,18] This virus is also found in Asia.[18]

An 'avian-like' H1N1 virus circulates in European pigs.[9,10,18] It seems to be an avian influenza virus that was transmitted whole to pigs and has replaced the classical H1N1 virus.[10,18] A different 'avian-like' H1N1 virus is co-circulating with the classical H1N1 virus in pigs in Asia.[18]

The H3N2 viruses that recently entered pigs in the Midwest are triple reassortants.[10,14,26] They contain hemagglutinin and neuraminidase proteins from a human influenza virus, and internal proteins from the classical swine influenza virus, an avian influenza virus and a human influenza virus.[26]

The H3N2 viruses in Europe and Asia seem to be the result of reassortment between a human H3N2 virus, circulating there in pigs since the 1970s, and the H1N1 'avian-like' virus.[9] These H3N2 viruses contain human N3 and N2 proteins, and internal proteins from the avian virus.[9]

The H1N2 virus in the U.S. is a reassortant of the classical H1N1 swine influenza virus and the triple reassortant H3N2 virus circulating in the U.S.[9]

The H1N2 virus in Europe is a reassortant of a human H1N1 virus and the 'human-like' European H3N2 virus.[9,18]

Equine influenza viruses

Equine influenza viruses mainly infect horses and other Equidae.[4,12,27] There is less antigenic drift in equine viruses than human viruses.[4,11] The two subtypes known to cause disease in horses are H7N7 (equine virus 1) and H3N8 (equine virus 2).[4,11,12] The H7N7 virus is currently extinct or present at only very low levels in some parts of the world.[4,12]

In 1989, a novel strain of equine influenza [A/eq/Jilin/89 (H3N8)] caused a serious epidemic, with high morbidity and mortality rates, in Chinese horses.[4] The virus appears to be an avian influenza virus. A related virus caused influenza in a few hundred horses the following year but there were no deaths. The avian-like virus continued to circulate in horses in China for at least 5 years without further fatalities.

Human influenza viruses

Human influenza viruses are mainly found in humans, but also infect ferrets and sometimes swine.[11,12,18,28-32] H1N1, H1N2 and H3N2 viruses are currently in general circulation in humans.[3,33] The H1N2 viruses appeared in 2001, probably as a result of genetic reassortment between the H3N2 and H1N1 viruses.[33,34] H2N2 viruses circulated in the human population between 1957 and 1968.[12]

Human influenza viruses change frequently as the result of antigenic drift, and occasionally as the result of antigenic shift. Epidemics occur every few years, as a result of small changes in the influenza viruses.[9,35] Human pandemics, resulting from antigenic shift, were most recently reported in 1918, 1957 and 1968.

Influenza viruses in other species

H7N7 and H4N5 viruses, closely related to avian viruses, have been isolated from seals.[12] In 1984, a H10N4 virus was isolated from mink during an epidemic in Sweden.[12] This virus is thought to have been of avian origin. A H5N1 avian influenza virus was recently isolated from sick domestic and zoo cats in Asia.[15,17]

Influenza B viruses

Influenza B viruses are not categorized into subtypes, but are classified into strains.[3]

Influenza B viruses undergo antigenic drift but not antigenic shift.[3] Antigenic drift is slower in influenza B than in influenza A viruses.[12,33] Influenza B viruses can cause epidemics in humans, but have not, to date, been responsible for pandemics.[12] They have also been found in animals.[9,12,23,29,36]

Influenza C viruses

Influenza C viruses are not classified into subtypes, but are classified into strains.[3]Each strain is antigenically stable, and accumulates few changes over time.[37] However, recent evidence suggests that reassortment does occur frequently between different strains of influenza C viruses.[37,38] Type C viruses can cause mild disease in humans, but have never been associated with large scale epidemics.[8,12,35,39] They have also been found in animals.[9,11,12,23,29,39,40-42]

Geographic Distribution

Human and avian influenza viruses are found worldwide.[2,11-13] Avian HPAI viruses have been eradicated from domestic poultry in most developed nations, but are found worldwide in waterfowl.[2] In North America, H3, H4 and H6 viruses are found most often in wild ducks, but H5, H7 and H9 viruses are also found at low levels.[43]

In early 2004, widespread outbreaks of an avian influenza H5N1 (HPAI) virus occurred in poultry in Cambodia, China, Indonesia, Japan, Laos, South Korea,

Thailand and Vietnam.[3] Beginning in June 2004, new outbreaks of a H5N1 (HPAI) virus were reported in poultry in China, Indonesia, Thailand and Vietnam. Human, feline and possibly porcine infections and deaths have been associated with these outbreaks.

Swine influenza is common in North and South America, Europe and Asia and has been reported from Africa.[18,23] Although the subtypes of the swine influenza viruses found in the U.S. and Europe are the same, they are actually different viruses (see 'Etiology').

Only Australia, New Zealand and Iceland are known to be free from equine influenza.[27] The H3N8 subtype is widespread in horse populations.[4] The H7N7 subtype may be either extinct or present at only very low levels in some parts of the world, including the North America and Europe.[4,12,27] It can still be found at low levels in Central Asia.[12]

Transmission

In mammals, the influenza viruses are transmitted in aerosols created by coughing and sneezing, and by contact with nasal discharges, either directly or on fomites.[4,11,12,18,25,33,35] Close contact and closed environments favor transmission. Influenza viruses are relatively labile, but can persist for several hours in dried mucus.[35] In ferrets, *in utero* transmission can occur with high viremia after experimental infection.[32]

In birds, avian influenza viruses are shed in the feces as well as in saliva and nasal secretions; fecal-oral transmission is the most common means of spread.[2,3,11,12] Waterfowl can carry the avian influenza viruses asymptomatically and transmit them to poultry.[2,11] Viruses have also been found in the yolk and albumen of eggs from infected hens.[2] Although these eggs are unlikely to hatch, broken shells could transmit the virus to other chicks in the incubator. Fomites can be important in transmission and flies may act as mechanical vectors.[2,19,20]

Recently, avian influenza H5N1 was reported in domestic and zoo cats during an outbreak in Asia.[15,17] The cats were all thought to have been infected by eating raw infected poultry. Experimental infections were established in cats by intratracheal inoculation with H5N1 viruses and by feeding H5N1-infected chicks.[17]

Avian influenza viruses (H7N2, LPAI) can persist for up to 2 weeks in feces and on cages.[44] They can also survive for up to 32 days at 15–20°C, and at least 20 days at 28–30°C, but are inactivated more quickly when mixed with chicken manure.[44] HPAI viruses can survive indefinitely when frozen.[19] The avian viruses have also been isolated from the water in ponds where ducks swim.[9,12]

Transmission between species

Ordinarily, swine influenza viruses circulate only among pigs, equine influenza viruses among the Equidae, avian influenza viruses among birds, and human influenza viruses among humans. Occasionally, these viruses cross species barriers. Generally, the virus is not well adapted to the new host species and does not undergo sustained transmission.[3,10-12,23]

Transmission of the avian influenza viruses to people is rare, and has been reported only with the H5, H7 and H9 viruses.[3,7] Most infections have been the result of direct contact with infected poultry or fomites; however, during a 2003 outbreak in the Netherlands, three human infections occurred in family members of infected poultry workers.[3,5] The virus subtype was H7N7. No cases of sustained person-to-person transmission with the avian viruses have been reported, to date.

The H5N1 avian influenza viruses may be likely to undergo cross-species transmission. These viruses have been isolated at least 56 times in humans, after contact with infected poultry.[3,9,14,19,20,45] They have also been isolated recently from cats that ate infected poultry.[15,17] Cats, pigs and mice have been experimentally infected.[14,17] In addition, preliminary evidence of natural infections with the H5N1 viruses has been reported for the first time in pigs, in Fujian province, China.[14]

Infections with swine influenza viruses have been reported sporadically in humans in the U.S., Europe and New Zealand.[7,9,12,24,46] One college student transmitted the virus to his roommate, who remained asymptomatic.[24] Limited person-to-person transmission was also reported in 1976, when approximately 500 military recruits in Fort Dix, New Jersey were infected with a swine influenza virus.[9,12,24] This virus spread to a limited extent on the base, which contained approximately 12,000 people, but did not spread to the surrounding community. Recent serologic evidence suggests that swine influenza infections may occur regularly in people who have contact with pigs.[7,9,12] If these infections resemble human influenza, they may not be recognized or reported as caused by a swine influenza virus.

Pigs are readily infected with human influenza A viruses, but most strains do not spread widely.[12] Pigs can also be infected with human influenza B viruses; serologic studies from the U.K. suggest that these infections are sporadic and do not spread to other pigs.[29]

Rarely, transmission between species results in an epidemic in the new host. Generally, this requires a novel hemagglutinin and/or neuraminidase protein to evade the immune response, together with viral proteins that are well adapted to the new host's cells.[10] Occasionally, a virus is transferred whole to the new host and can

spread. This has occurred a few times when avian viruses infected mink, horses, seals and pigs.[4,10,12,16,18] However, dissemination is more likely if the novel virus reassorts with a virus that is already adapted to the host species.[3] Reassortment can occur in the new host's own cells.[3,10,20] It could also occur in an intermediate host, particularly a pig.[3,9,10,20] Pigs have receptors that can bind swine, human, and avian influenza viruses.[7,9,18,25] For this reason, they have been called 'mixing vessels' for the formation of new viruses.

Although reassortment can occur anywhere, many of the new viruses originate in Asia. In rural China and other regions, a variety of species including ducks are kept in close proximity to each other and to humans.[9,12,14] This results in an increased opportunity for virus reassortment.

The last three human pandemics appear to have been the result of reassortments.[10]

The 1957 H2N2 ('Asian flu') virus contained avian hemagglutinin, neuraminidase and an internal protein, and 5 other proteins from a human H1N1 strain.[9,10] The H3N2 'Hong Kong flu' virus of 1968 had two new proteins from an avian virus – the new hemagglutinin and an internal protein - but kept the neuraminidase and remaining proteins from the H2N2 virus.[9,10] The origin of the strain that caused the 1918 human pandemic ('Spanish flu') is uncertain. Although the hemagglutinin protein is more closely related to avian influenza viruses than to human influenza viruses, there is some evidence that this virus may have evolved in an intermediate host before causing an epidemic in humans.[10] Repeated reassortments of human, avian and swine influenza viruses have also resulted in novel swine viruses (see 'etiology' for a description of these viruses).

Reassortant highly pathogenic avian influenza viruses may become progressively more virulent for mammals. From 1999 to 2002, H5N1 avian influenza viruses isolated from healthy ducks in southern China acquired the ability to replicate and cause lethal disease in mice.[14] Most of these viruses appear to be reassortants that contained a hemagglutinin gene related to the A/Goose/Guangdong/1/96 (H5N1) HPAI avian influenza virus and other genes from unknown Eurasian avian influenza viruses.

Disinfection

The influenza viruses are susceptible to a variety of disinfectants including 1% sodium hypochlorite, 70% ethanol, glutaraldehyde, formaldehyde and lipid solvents.[1,11,23,35]They can also be inactivated by heat of 56°C for a minimum of 30 min, radiation or pH 2.[1,11,35,44]

Infections in Humans

Incubation Period

The incubation period is usually short; most infections appear after one to four days.[12,33-35]

Clinical Signs

Uncomplicated infections with the human influenza A or B viruses are usually characterized by upper respiratory symptoms, which may include fever, chills, anorexia, headache, myalgia, weakness, sneezing, rhinitis, sore throat or a nonproductive cough.[8,12,32-35] Diarrhea, abdominal pain and photophobia have also been reported.[8,32] Nausea, vomiting and otitis media are common in children, and febrile seizures have been reported in severe cases.[33,34] In young children, the initial signs may mimic bacterial sepsis.[33] Most people recover in 1 to 5 days but, in some cases, the symptoms may last up to 2 weeks or longer.[8,33,35]

More severe symptoms, including pneumonia, can be seen in individuals with chronic respiratory or heart disease.[8,33-35] Secondary bacterial or viral infections may also occur.[8,12,33,34] In addition, influenza A has been associated with encephalopathy, transverse myelitis, Reye syndrome, myocarditis, pericarditis and myositis.[33,34]

Influenza C viruses are thought to mainly cause a mild upper respiratory disease in children and young adults, but more severe cases similar to influenza A or B have also been reported.[12,37-39] Some infections have resulted in bronchitis or pneumonia.[37] Infections may also be asymptomatic.

Avian influenza infections in humans

Rare infections with avian influenza viruses have been reported in humans. Healthy children and adults, as well as those with chronic medical conditions, have been affected.[20] While some infections have been limited to conjunctivitis and/or typical influenza symptoms, others were serious or fatal.[3,5,9,14,19,20,45,49] Viral pneumonia, acute respiratory distress syndrome, severe bronchointerstitial pneumonia, multiple organ dysfunction and other severe or fatal complications have been reported.[5,20] In one fatal case, the initial symptoms were limited to a persistent high fever and headache, and respiratory disease was not seen until later.[5] The HPAI viruses appear to cause more severe infections than the LPAI viruses.[3]

The following human infections have been reported recently:

- In 1997, eighteen human infections were reported in association with a H5N1 avian influenza virus outbreak in poultry in Hong Kong.[3,9,14,19,20] The symptoms included fever, sore throat and cough

and, in some cases, severe respiratory distress and viral pneumonia.[20] Eighteen people were hospitalized and six died.

- In 1999, avian influenza (H9N2) was confirmed in two children in Hong Kong.[3,14,20] The illnesses were mild and both children recovered. No other cases were found. Six unrelated H9N2 infections were also reported from mainland China in 1998-99; all six people recovered.[3,14]
- In 2002, antibodies to an avian H7N2 virus were found in one person after an outbreak in poultry in Virginia.[3]
- In 2003, two avian influenza H5N1 infections were reported in a Hong Kong family that had traveled to China.[3,14,20] One of the two people died. Another family member died of a respiratory illness while in China, but no testing was done.
- In 2003, 347 total and 89 confirmed human infections were associated with an outbreak of avian H7N7 influenza virus in poultry in the Netherlands.[3,5,14,49] Most cases occurred in poultry workers, but three family members also became ill.[3,5] In 78 of the confirmed cases, conjunctivitis was the only sign of infection.[5] Two people had influenza symptoms such as fever, coughing and muscle aches. Five had both conjunctivitis and influenza-like illnesses. (Four cases were classified as "other.") The single death occurred in an otherwise healthy veterinarian who developed acute respiratory distress syndrome and other complications.[5] His initial symptoms included a persistent high fever and headache but no signs of respiratory disease. The virus isolated from the fatal case had accumulated a significant number of mutations, while viruses from most of the other individuals had not.[5]
- Cases of conjunctivitis have been reported after contact with H7N7 avian viruses in infected seals.5,16
- In 2003, a H9N2 avian influenza virus infection was confirmed in a child in Hong Kong.[3,20] The child was hospitalized but recovered.
- In 2003, a H7N2 infection with respiratory signs was reported in a patient in New York.[3] The person, who had serious underlying medical conditions, was hospitalized but recovered.
- In 2004, two cases of conjunctivitis and flu-like symptoms were confirmed in poultry workers in Canada.[45] Both people recovered after treatment with an antiviral drug. Ten other infections were suspected but not confirmed; these cases included both conjunctivitis and upper respiratory symptoms. All of the infections were associated with a H7N3 virus outbreak in poultry.
- In 2004, human illness and deaths have been associated with widespread outbreaks of avian influenza (H5N1) among poultry in Asia. Twenty-two cases and 15 deaths were confirmed in Vietnam, and 12 cases with 8 deaths in Thailand through February 2004.[3] Deaths were not reported in other countries. An additional 3 deaths were reported in Vietnam in August, in association with new outbreaks of HPAI (H5N1) virus among poultry in China, Indonesia, Thailand and Vietnam.[45]

Swine influenza virus infections in humans

Although serologic evidence suggests that zoonotic infections with swine influenza viruses may not be uncommon, relatively few infections have been documented.[7] It is unknown whether infections with swine influenza viruses differ significantly from infections with human influenza viruses.[7]

Reported cases of influenza caused by swine influenza viruses include the following:

- A self-limiting illness with flu symptoms was reported in a college student.[24] There was evidence that his roommate had been infected but remained asymptomatic.
- An infection with flu symptoms including diarrhea was reported in a young boy, who recovered.[24] There was no evidence of spread to his family.
- Swine influenza virus was isolated from an immunocompromised child with pneumonia who died.[46] Serologic evidence of possible infection was found in five contacts, but the infection did not spread further.
- A localized outbreak was reported at Fort Dix, New Jersey. A swine influenza virus was isolated from 5 recruits with respiratory disease, including one who died of pneumonia.[9,12,24] Serologic evidence suggested that approximately 500 people on the fort had also been infected by person-to-person spread.

Equine influenza virus infections in humans

Antibodies to the equine H3N8 viruses have been reported in humans.[12] Human volunteers inoculated with an equine virus became ill, and virus could be isolated for up to 10 days.[12]

Communicability

The human influenza viruses are readily transmitted from person to person. Infected adults usually begin to shed influenza A viruses the day before the symptoms appear, and are infectious for 3 to 5 days after the initial signs.[33,35] Young children can shed virus for up to 6 days before, and more than 10 days after they become ill.[33,34] Severely immunocompromised individuals may remain infectious for weeks to months.[33,34] Humans can transmit influenza viruses to ferrets and, occasionally, to swine.[11,12,28,31]

Rare cases of person-to-person spread, including a localized outbreak among recruits at a military base, have been reported in humans infected with swine influenza viruses.[9,12,24] Rare cases of probable person-to-person transmission, and no cases of sustained transmission, have been reported in humans infected with the avian influenza viruses.[3,5]

Diagnostic Tests

In humans, influenza A and B can be diagnosed by virus isolation, detection of antigens or nucleic acids, or retrospectively by serology. The viruses can be isolated in cell lines or chicken embryos, and are identified by hemagglutination inhibition tests.[8,12] Antigens can be detected in respiratory secretions by immunofluorescence or ELISAs.[8,34] Commercial rapid diagnostic test kits (Directigen® Flu A test) can provide a diagnosis within 30 minutes.[34] PCR techniques are also available.[33,34] Serologic tests include complement fixation, hemagglutination inhibition, and immunodiffusion.[8,12,34] A rising titer is necessary to diagnose influenza by serology.

Avian influenza viruses can be identified by PCR, antigen detection or virus isolation.[3] In the U.S., samples that test positive by PCR or antigen tests are confirmed by the Centers for Disease Control and Prevention (CDC). PCR and antigen testing of avian influenza viruses must be carried out in Biosafety Level (BSL) 2 laboratory conditions.[3] BSL 3+ laboratory conditions are needed for isolation of the HPAI viruses.[3]

Treatment

Four antiviral drugs are available for influenza treatment in the U.S. Amantadine and rimantadine are active against influenza A viruses, if treatment is begun within the first 48 hours.[8,33,35,50] Zanamivir and oseltamivir are effective for both influenza A and influenza B.[33,50] Treatment usually results in milder symptoms and recovery, on average, one day sooner.[8,33,50]

Drug resistance develops rapidly in viruses exposed to amantadine or rimantadine, and may emerge during treatment.[8,12,33] Some of the H5N1 viruses isolated in 2004 in Asia have been resistant to amantadine and rimantadine. Laboratory studies have shown that influenza viruses can also become resistant to zanamivir and oseltamivir.[33,50]

Prevention

An annual vaccine is available for influenza A and B.[8,12] Both inactivated (injected) and live (intranasal) vaccines may be available.[33] The vaccine is given in the fall before the flu season.[8] It contains the strains of viruses thought most likely to produce epidemics during the following winter, and is updated annually. Details on vaccine efficacy, vaccine types, and recommendations for vaccination in specific population groups are available from the CDC.[34]

Three antiviral drugs - amantadine, rimantadine and oseltamivir - can be used for prophylaxis in high risk populations such as the elderly or immunocompromised.[33,34,50]

Other preventative measures include avoidance of contact with people with symptomatic disease, as well as hand washing and other hygiene measures. People with influenza should avoid contact with ferrets.[31] If contact is unavoidable, they should wear gloves and face masks to prevent transmitting the virus to the animal.[28]

Preventative measures for the avian influenza viruses

The control of epidemics in poultry decrease the risk of exposure for humans.[20] People working with infected birds should follow good hygiene practices and wear protective clothing, including boots, coveralls, gloves, face masks and headgear.[19,20] In addition, the World Health Organization (WHO) recommends prophylaxis with antiviral drugs in people who cull birds infected with H5N1 HPAI viruses.[20]

To prevent reassortment between human and avian influenza viruses, people in contact with infected birds should be vaccinated against human influenza.[10,20] They are also discouraged from having contact with sick birds while suffering flu symptoms.[10]

Morbidity and Mortality

Although the morbidity rates for influenza are high, uncomplicated infections with the human viruses are rarely fatal in healthy individuals.[8,10,12,32,35] Infections are more severe in the elderly, young children (particularly infants), people with respiratory or cardiac disease, and those who are immunosuppressed.[8,33-35] Influenza-related deaths are usually the result of pneumonia or the exacerbation of a cardiopulmonary condition or other chronic disease.[34] Over 90% of these deaths occur in the elderly.[33] The estimated mortality rate from influenza is 0.0004-0.0006% in persons from 0-49 years old, 0.0075% between the ages of 50 and 64, and 0.1% in those over 65.[33,34] Deaths are rare in children, but can occur.[33,34] Immunity to the viral surface antigens reduces the risk of infection and severity of disease. Antibodies offer limited or no protection against other virus types or subtypes.[33]

Human influenza can occur as a localized outbreak, an epidemic, a pandemic, or as sporadic cases.[10] Although a new virus may spread among a population before the "flu season," epidemics in temperate regions usually do not begin until after school starts in the fall.[8] During a typi-

cal epidemic, influenza appears first among school-aged children, then spreads to preschool children and adults.[8,12] During epidemics, 15% to 40% of the population may be infected.[10,12] The outbreak usually lasts for 3 to 6 weeks.[8,12] Epidemics in tropical regions are not usually seasonal.[12]

Antigenic drift is usually responsible for small scale epidemics and localized outbreaks.[9] In North America, an epidemic of influenza A usually occurs every 1 to 3 years, and an epidemic of influenza B every 3 to 4 years.[35] Since 1968, the type A (H3N2) viruses have caused the most serious outbreaks with the highest mortality rates.[33,34] Influenza C viruses cause sporadic cases of influenza and minor localized outbreaks, but have not, to date, been associated with epidemics.[8,12,35,39]

Severe pandemics, which last occurred in 1918, 1957 and 1968, are caused by antigenic shifts in influenza A viruses.[8,10] During influenza pandemics, the morbidity and mortality rates can increase dramatically in all age groups.[3,8,9,12,18,34] In the most severe pandemic, in 1918, the morbidity rate was 25-40% and the case fatality rate 2-5%.[10] Approximately 500,000 deaths were reported in the U.S. and an estimated 20-50 million deaths worldwide.[3,8-10,12,18] After a pandemic, an influenza virus usually becomes established in the population and circulates for years.[3]

Zoonotic influenza

Human infections with avian influenza viruses are rarely reported. The severity of the disease seems to depend on the virus subtype and strain. More severe infections have been reported with the HPAI viruses, particularly H5N1. From 1997 to 2004, there were at least 56 confirmed H5N1 virus infections, and 33 of these cases were fatal.[3,9,14,19,20,45] Human disease has also been reported after infections with H7N2, H7N3, H7N7 and H9N2 viruses.[3,5,14,16,45,49] Most infections with the H7 viruses have been limited to conjunctivitis, but influenza symptoms have also been seen. A single death was seen in an otherwise healthy veterinarian who became infected with a H7N7 virus.[5]

Most humans infected with the swine influenza viruses have had mild disease or been asymptomatic, but three deaths were reported: one in a young boy who was immunosuppressed, one in a military recruit and one in a pregnant woman who developed pneumonia.[9,12,24,46] During the only known outbreak, on a military base in New Jersey, the swine influenza virus was isolated from 5 people with respiratory disease, including one who died of pneumonia, and serologic evidence of infection was found in approximately 500 of 12,000 people on the base.[9,12,24] Serologic evidence also suggests that people who work with pigs are occasionally infected with swine influenza viruses, but these infections may not be reported if they resemble human influenza.[7,9,12]

Infections in Animals

Species Affected

Influenza A Viruses

Influenza A viruses can cause disease in birds, swine, horses, ferrets, mink, seals, whales, humans and other species.

Avian influenza viruses mainly infect birds, but can also cause disease in horses, swine, mink, cats, marine mammals and humans.[3,4,9,10,12,15-18] Waterfowl appear to be the natural reservoirs for the influenza A viruses.[2,9,12,18,20] Most, but not all, infections in wild birds are asymptomatic.[2,3,9,12] Poultry can develop serious or mild disease, depending on the subtype and strain of virus.[2,22] In cage birds, most infections have been recorded in passerine birds.[22] Psittacine birds are rarely affected.

Swine influenza viruses mainly affect pigs but can also cause disease in turkeys and humans.[7,11,12,23]

Equine influenza viruses mainly affect horses, donkeys and other Equidae.[4,27] Antibodies to the equine H3N8 viruses have been reported in humans.[12]

Human influenza viruses mainly cause disease in humans and ferrets.[28,30-32] They can also infect pigs and have been reported in dogs, cattle and birds.[11,12,29] Experimental infections have been reported in horses.[12]

Influenza B viruses

Influenza B viruses can cause disease in humans, ferrets and seals, however these viruses have also been isolated from pigs and a horse.[9,12,23,36] Serologic evidence of infection has been found in pigs, dogs and horses.[12,29]

Influenza C viruses

Influenza C viruses have been isolated from humans and swine.[9,11,12,23,39,40] These viruses can cause disease in experimentally infected dogs.[12] Serologic evidence of infection has been found in pigs, dogs and horses.[12,29,41,42]

Incubation Period

The incubation period is generally short. The clinical signs usually appear within 1 to 3 days in horses, pigs or seals.[4,11,12,23,25,27,47] Rarely, incubation periods up to 7 days have been reported in some horses.[27] In poultry, the incubation period can be a few hours to a week.[2,11,13]

Clinical Signs

Avian influenza

The highly pathogenic avian influenza (HPAI) viruses cause severe disease in poultry. These viruses can cause serious infections in some species of birds on a farm

while leaving others unaffected.[2,12] The clinical signs are variable.[2,6,11,22] The typical symptoms are those of a respiratory disease with sinusitis, lacrimation, edema of the head, cyanosis of the head, comb and wattle, and green to white diarrhea.[2,6,11,13,19] Hemorrhagic lesions may be found on the comb and wattles of turkeys.[2,11] Other signs may include anorexia, coughing, sneezing, blood-tinged oral and nasal discharges, ecchymoses on the shanks and feet, neurologic disease, decreased egg production, loss of egg pigmentation and deformed or shell-less eggs.[2,11-13, 19] Sudden death may occur with few other signs.[6] Most of the flock usually dies.[2] In ducks, the most common symptoms are sinusitis, diarrhea and increased mortality.[2,11]

The low pathogenic (LPAI) viruses usually cause subclinical or mild illness.[22] The symptoms may include decreased egg production or increased mortality rates.[3,13] More severe disease, mimicking highly pathogenic avian influenza, can be seen if the birds are concurrently infected with other viruses or there are other exacerbating factors.[6,22]

Turkeys infected with swine influenza viruses may develop respiratory disease, have decreased egg production, or produce abnormal eggs.[11]

Avian influenza is often subclinical in wild birds, but some strains can cause illness and death.[2,3,9,12]

Swine influenza

Swine influenza is an acute upper respiratory disease characterized by fever, lethargy, anorexia, weight loss and labored breathing.[9,11,12,23,25] Coughing may be seen in the later stages of the disease.[9] Sneezing, nasal discharge and conjunctivitis are less common symptoms.[9] Abortions may also occur.[23,25] Some virus strains can circulate in pigs with few or no clinical signs.[9,12,18] Recovery usually occurs after 3 to 7 days.[9,11,23]

Complications may include secondary bacterial or viral infections.[9,25] Severe, potentially fatal bronchopneumonia is occasionally seen.[11]

Equine influenza

Equine influenza usually spreads rapidly in a group of animals. In naïve horses, the first sign is usually a fever, followed by a deep, dry cough.[4] Other symptoms may include a serous to mucopurulent nasal discharge, myalgia, inappetence and enlarged submandibular lymph nodes.[4,11,12,27] There may be edema of the legs and scrotum, and spasmodic impaction colic has been reported.[4,27] Animals with partial immunity can have milder, atypical infections with little or no coughing or fever.[4]

Healthy adult horses usually recover within 1-2 weeks, but the cough may persist longer.[4,12,27] Secondary bacterial infections prolong recovery.[4,11,27] Death in adult horses usually results from bacterial pneumonia, pleuritis or purpura hemorrhagica.[4] Sequelae may include chronic pharyngitis, chronic bronchiolitis and emphysema.[4,27] Interstitial myocarditis can occur during or after the infection.[12] Young foals without maternal antibodies can develop a rapidly fatal viral pneumonia.[4,12]

Horses experimentally infected with human influenza virus (H3N2 'Hong Kong') developed a mild febrile illness.[12] The virus could be isolated for up to 5 days.

Influenza in ferrets

Ferrets are susceptible to the human influenza viruses. The symptoms may include fever, anorexia, depression, listlessness, sneezing, purulent nasal discharge and coughing.[28,30,32] The infection is not usually fatal in adult animals, which generally recover in 5 days to 2 weeks.[28,31,32] More severe or fatal disease can be seen in neonates.[32]

Influenza in mink

In 1984, a H10N4 avian influenza virus caused an epidemic on 33 mink farms in Sweden.[12] The symptoms included anorexia, sneezing, coughing, nasal and ocular discharges, and numerous deaths.

H5N1 influenza in cats

Influenza A was recently reported in cats. During an epidemic of H5N1 avian influenza in Asian poultry, there were anecdotal reports of fatal influenza in domestic cats, a white tiger and a clouded leopard.[15] H5N1 avian influenza virus was isolated from these animals, which were all thought to have been infected by eating raw, infected poultry.

Clinical signs in cats experimentally infected with the H5N1 virus included fever, lethargy, conjunctivitis, protrusion of the third eyelid and dyspnea.[17] One cat died on the 6th day after inoculation; the remaining animals were euthanized and necropsied the following day. There was no evidence of infection after inoculation with a human H3N2 virus.[17]

Influenza in marine mammals

Influenza A viruses have been associated with outbreaks of pneumonia in seals and disease in a pilot whale.[12,16,47] The viruses appear to be of avian origin.[16] Clinical signs in seals have included weakness, incoordination, dyspnea and swelling of the neck.[47] A white or bloody nasal discharge was seen in some animals. In the single known case in a whale, the symptoms included extreme emaciation, difficulty maneuvering and sloughing skin.[47]

Influenza in dogs

The clinical signs in dogs experimentally infected with influenza C virus included nasal discharge and conjunctivitis, which persisted for 10 days.[12]

Communicability

Influenza viruses are readily transmitted between animals in the same species. More rarely, they can be transmitted to other species. Pigs may begin excreting influenza viruses within 24 hours of infection and typically shed the viruses for 7 to 10 days.[18,25] Shedding up to 4 months has been documented in one pig.[18] Horses begin excreting the virus during the incubation period and usually excrete the virus for 4 to 5 days or less after the onset of clinical signs.[4,11] Most chickens shed LPAI influenza viruses for only a week, but a minority of the flock can excrete the virus in the feces for up to 2 weeks.[44] Ducks can shed avian influenza viruses for up to 30 days.[9]

Cats experimentally infected with the avian influenza H5N1 virus shed the virus by the third day post-inoculation, and were able to infect two sentinel cats in close contact.[17]

Diagnostic Tests

Avian influenza

Avian influenza is usually diagnosed by virus isolation in embryonated eggs.[6,13] The virus can be isolated from tracheal, oronasal or cloacal swabs in live birds, and pooled or individual organ samples (trachea, lungs, air sacs, intestine, spleen, kidney, brain, liver and heart) from dead birds.[2,6] Feces can be substituted in small birds if cloacal samples are not practical. The virus is subtyped with immunodiffusion tests, or hemagglutination and neuraminidase inhibition tests.[6] Virus inoculation into susceptible birds, together with genetic tests, is used to differentiate LPAI from HPAI viruses.[6]

Viral antigens can be detected with ELISAs, including a rapid test (Directigen® Flu A kit, Becton Dickinson Microbiology Systems).[6] Reverse transcription polymerase chain reaction (RT-PCR) tests may be used to identify nucleic acids.[6] Serological tests, including agar gel immunodiffusion, hemagglutination inhibition and ELISAs, may be used as supplemental tests.[6]

Swine influenza

Swine influenza can be diagnosed by virus isolation, detection of viral antigens or nucleic acids, and serology. Mammalian influenza viruses can be isolated in embryonated chicken eggs or cell cultures.[9,25] The swine influenza viruses can be recovered from lung tissues at necropsy, or nasal or pharyngeal swabs from acutely ill pigs.[11,23,25] Recovery is best from an animal with a fever, 24-48 hours after the onset of disease.[25] Isolated viruses are subtyped with hemagglutination inhibition and neuraminidase inhibition tests.[9,25]

Immunofluorescent techniques can detect antigens in fresh lung tissue, nasal epithelial cells or bronchoalveolar lavage.[9,25] Other antigen tests include immunohistochemistry on fixed tissue samples, and ELISAs including the Directigen® Flu A test.[9,25] RT-PCR assays are also available.[9,25]

Serology on paired samples can diagnose swine influenza retrospectively.[23] The hemagglutination inhibition test, which is subtype specific, is most often used.[9,23,25] It may not detect new viruses.[9] ELISA tests are also used. Rarely used serological tests in swine include agar gel immunodiffusion, the indirect fluorescent antibody test and virus neutralization.[25]

Equine influenza

Equine influenza may tentatively be diagnosed based on the clinical signs.[27] As in swine, the disease is confirmed by virus isolation, the detection of viral antigens or nucleic acids, or retrospectively by serology.[4,27] In horses, peak virus shedding is thought to occur during the first 24 to 48 hours of fever.[4]

As in swine, a serological diagnosis requires paired acute and convalescent samples.[4] The most commonly used tests in horses are the hemagglutination inhibition test and a single-radial hemolysis (SRH) test.[4] An ELISA that can distinguish natural from vaccine-induced antibodies is in development.[4]

Treatment

Animals with influenza are usually treated with supportive care and rest.[4,13,23,27] Antibiotics may be used to control secondary infections.[4,13,27] Antiviral drugs are not generally given to animals, but could be of use in valuable horses.[2]

Poultry flocks with highly pathogenic avian influenza are depopulated and are not treated.[3,11]

Prevention

Inactivated influenza vaccines are available for pigs, horses and, in some countries, birds.[4,11,12,23,25,27] The vaccines do not always prevent infection, but the disease is usually milder if it occurs. In the U.S., avian influenza vaccines are used most often in turkeys and are intended only to prevent infection by LPAI viruses.[6] HPAI vaccines are not used routinely in the U.S. or most other countries.[6] A "DIVA" (differentiating infected from vaccinated animals) strategy has been successfully used to control a low pathogenicity avian influenza outbreak in Italy.[48] This strategy depends on using an inactivated vac-

cine containing the homologous H type and a heterologous N type. Vaccinated birds that subsequently become infected can be detected by testing for antibodies to the N type of the field strain.

Influenza vaccines change periodically to reflect the current subtypes and strains in a geographic area. In general, swine and equine viruses display less antigenic drift than human viruses and these vaccines are changed less often.[4,9,11] Avian vaccines are usually autogenous or from viruses of the same subtype or hemagglutinin type.[6]

Poultry can be infected by contact with newly introduced birds or wild birds, particularly waterfowl.[9,11,19,20] The risk of infection can be decreased by all-in/ all-out flock management, and by preventing any contact with wild birds or their water sources.[2,19] Biosecurity measures can prevent the entry of the virus on fomites.[2,19,20] Birds should not be returned to the farm from live bird markets or other slaughter channels.[19]

In pigs and horses, influenza is usually introduced into a facility in a new animal.[9,11,18,23,27] Isolation of newly acquired animals can decrease the risk of transmission to the rest of the herd.[27] The virus usually persists in an infected swine herd and causes periodic outbreaks, but good management can decrease the severity of disease.[9,12,18,23] Infected swine herds can be cleared of influenza viruses by depopulation.[18]

Ferrets can be infected by the human influenza viruses; people with influenza should avoid contact with ferrets.[31] If contact is unavoidable, a face mask and gloves should be worn.[28]

Cats should not be fed poultry infected with the avian influenza viruses.[15]

Prevention of virus transmission during outbreaks

During an outbreak of influenza among mammals, quarantines and isolation of infected animals help prevent virus dissemination.[4,11] Good hygiene can keep the virus from spreading on fomites. Rest decreases virus shedding in horses.[4] Infected facilities should be cleaned and disinfected after the outbreak.

In poultry, outbreaks of highly pathogenic avian influenza are controlled by eradication.[3,11] The outbreak is managed by quarantine, depopulation, cleaning and disinfection, and surveillance around the affected flocks. Strict hygiene is necessary to prevent virus transmission on fomites.

Morbidity and Mortality

The severity of an influenza virus infection varies with the dose and strain of virus and the host's immunity. In mammals, uncomplicated infections are usually associated with high morbidity rates, low mortality rates and rapid recovery.[4,9,11,12,23,25,27] Secondary bacterial infections can exacerbate the symptoms, prolong recovery and result in complications such as pneumonia.

Swine influenza

Influenza is a major cause of acute respiratory disease in finishing pigs. Approximately 25-33% of 6-7 month old finishing pigs and 45% of breeding pigs have antibodies to the classical swine H1N1 virus in the U.S.[12,18] High seroprevalence rates to swine influenza viruses have also been reported in other countries.[9,12,18,29] In addition, pigs can be infected with the human influenza A, B and C viruses.[9,11,12,23,29,39,40,42] In the U.K., a study found antibodies to both swine and human influenza viruses in 14% of all pigs.[18] Approximately 10% of the pigs were seropositive for influenza C viruses, but only sporadic infections with the human influenza B viruses were found.[29] In Japan, a similar study found antibodies to the type C viruses in 19% of pigs.[42]

Swine influenza viruses are usually introduced into a herd in an infected animal, and can survive in carrier animals for up to 3 months.[11,18,23] In a newly infected herd, up to 100% of the animals may become ill but most animals recover within 5 to 7 days if there are no secondary bacterial infections or other complications.[9,11,23,25] In uncomplicated cases, the case fatality rate has ranged from less than 1% to 3%.[11,12]

Once the virus has been introduced, it usually persists in the herd.[9,12,18] Annual outbreaks are often seen, and occur mainly during the colder months.[9,12,18,23] Many of the infections in endemically infected herds are subclinical; typical signs of influenza may occur in only 25% to 30% of the pigs.[9,18] Maternal antibodies decrease the severity of disease in young pigs.[9] Some viruses can infect the herd with few or no clinical signs.[9,12,18]

Influenza epidemics can occur if a virus infects a population without immunity to the virus, or if the infection is exacerbated by factors such as poor husbandry, stress, secondary infections or cold weather.[12,18] In the epidemic form, the virus spreads rapidly in pigs of all ages.[25] In a 1918 epizootic, millions of pigs developed influenza, and thousands of the infections were fatal.[12] Recently, a novel H3N2 entered pigs in the Midwest and has caused serious illness and reproductive losses in sows.[9]

Equine influenza

In horses, influenza outbreaks are not as seasonal as they are in pigs or humans.[4] Most outbreaks are associated with sales, races and other events where horses congregate.[4,11] Widespread epidemics can be seen, with morbidity rates up to 60-90%, in naïve populations. [4,12] In 1987, an equine influenza epidemic in India affected

more than 27,000 animals and killed several hundred.[4] In populations that have been previously exposed, cases are seen mainly in young and newly introduced animals.[4,12]

Unless there are complications, healthy adult horses usually recover within 1-2 weeks, although coughing can persist.[4,12,27] The H3N8 viruses usually cause more severe disease than the H7N7 viruses.[4,12] Deaths are rare in adult horses, and are usually the result of secondary bacterial infections.[4,12,27] Higher mortality rates have been reported in foals, animals in poor condition and donkeys.[4,27] A rapidly fatal viral pneumonia may be seen in young foals with no maternal antibodies.[4,12] In horses, tracheal clearance rates can be depressed for up to a month after infection.[4]

Avian influenza viruses have rarely been reported in horses. In 1989, a novel strain of equine influenza [A/eq/Jilin/89 (H3N8)] caused a serious epidemic in Chinese horses.[4] The morbidity rate was 80% and the mortality rate was 20%. The virus appeared to be an avian influenza virus. A related virus caused influenza in a few hundred horses the following year but there were no deaths. The avian-like virus continued to circulate in horses for at least 5 years without further fatalities.

Influenza in other mammals

In 1984, an outbreak with an avian H10N4 virus was reported on Swedish mink farms. The outbreak affected 33 farms and killed 3,000 mink.[12] The morbidity rate was nearly 100%.

Fatal infections with an avian H5N1 virus were recently reported in 3 domestic cats, a white tiger and a clouded leopard.[15] Experimental infections were also reported in 8 cats.[17] The morbidity and mortality rates are unknown. Cats inoculated with a human H3N2 virus had no evidence of virus replication or disease.[17]

In seals, the case fatality rate was estimated to be 20% in one outbreak with a H7N7 virus, and 4% in an outbreak with a H4N5 virus.[12] Explosive epidemics in seals are thought to be exacerbated by high population densities and unseasonably warm temperatures.[47]

Avian influenza

Avian influenza outbreaks occur in most countries including the U.S. Low pathogenic forms are seen most often, but outbreaks with the highly pathogenic H5 and H7 viruses are also reported periodically.[2,3] In poultry, HPAI viruses are associated with very high morbidity and mortality rates, up to 90-100%.[2,3] Any surviving birds are usually in poor condition. LPAI viruses usually result in mild or asymptomatic infections, but may also mimic HPAI viruses.[6,22]

Symptomatic infections and outbreaks have been reported in wild birds, but are unusual.[2,3,9,12]

Post-Mortem Lesions

Avian influenza

The lesions in poultry are highly variable and can resemble other avian diseases.[2] There may be subcutaneous edema of the head and neck, fluid in the nares and oral cavity, and severe congestion of the conjunctivae. Hemorrhagic tracheitis can be seen in some birds; in others, the tracheal lesions may be limited to excess mucoid exudate. Petechiae may be found throughout the abdominal fat, serosal surfaces and peritoneum. Hemorrhages may also be seen on the mucosa of the proventriculus, beneath the lining of the gizzard, and in the intestinal mucosa. The kidneys can be severely congested and are sometimes plugged with urate deposits. The ovaries may be hemorrhagic or degenerated, with areas of necrosis. The peritoneal cavity often contains yolk from ruptured ova. Severe airsacculitis and peritonitis may be seen in some birds. In birds that die peracutely and in young birds, the only lesions may be severe congestion of the musculature and dehydration.

Swine influenza

In uncomplicated infections, the gross lesions are mainly those of a viral pneumonia.[9] Affected parts of the lungs are depressed and consolidated, dark red to purple-red, and sharply demarcated.[9,23] The lesions may be found throughout the lungs but are usually more extensive in the ventral regions.[9] Other parts of the lungs may be pale and emphysematous.[23] The airways are often dilated and filled with mucopurulent or blood-tinged, fibrinous exudate.[23] The bronchial and mediastinal lymph nodes are typically enlarged.[9,23] Severe pulmonary edema, or serous or serofibrinous pleuritis may also be seen.[23] Some strains of swine influenza viruses produce more marked lesions than others.[9] Generalized lymphadenopathy, hepatic congestion and pulmonary consolidation were reported in one outbreak of severe disease in swine.[12]

Equine influenza

Interstitial pneumonia, pleuropneumonia, bronchitis, perivasculitis and interstitial myocarditis have been reported in fatal cases in horses.[27]

Influenza in cats

The lesions reported in experimentally infected cats were multiple to coalescing foci of pulmonary consolidation.[17] The lesions were similar whether the cats were infected intratracheally or by the ingestion of infected chicks.

Influenza in marine mammals

In seals, pneumonia with necrotizing bronchitis, bronchiolitis and hemorrhagic alveolitis have been reported.[16,47] In a single case in a whale, the lungs were hemorrhagic and a hilar lymph node was greatly enlarged.[47]

Internet Resources

Animal Health Australia. The National Animal Health Information System (NAHIS) http://www.aahc.com.au/nahis/disease/dislist.asp

Centers for Disease Control and Prevention (CDC) http://www.cdc.gov/flu/

Material Safety Data Sheets–Canadian Laboratory Center for Disease Control http://www.hc-sc.gc.ca/pphb-dgspsp/msds-ftss/index.html#menu

Medical Microbiology http://www.gsbs.utmb.edu/microbook

OIE Manual of diagnostic tests and vaccines for terrestrial animals http://www.oie.int/eng/normes/mmanual/a_summry.htm

Prevention and control of influenza. Recommendations of the Advisory Committee on Immunization Practices (ACIP) http://www.cdc.gov/mmwr/preview/mmwrhtml/rr5306a1.htm

The Merck Manual http://www.merck.com/pubs/mmanual/

The Merck Veterinary Manual http://www.merckvetmanual.com/mvm/index.jsp

USAHA Foreign Animal Diseases book http://www.vet.uga.edu/vpp/gray_book/FAD/

World Organization for Animal Health (OIE) http://www.oie.int/

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Newcastle Disease

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Importance

Newcastle disease produces a wide range of clinical signs in avian species, from mild to severe. Exotic Newcastle disease (END), the most severe form with neurologic and gastrointestinal signs, is not endemic in the United States. Frequent outbreaks do occur in the U.S. due to illegal importation of exotic birds. The disease is highly contagious and can have high mortality rates. Chickens are highly susceptible and economic losses can be significant.

Etiology

Newcastle disease viruses are classified in the serotype group avian paramyxovirus type 1 (APMV–1) in the genus Rubulavirus, family Paramyxoviridae. There are nine avian paramyxovirus serotypes designated APMV–I to APMV–9.

Species affected

Many avian species are affected by Newcastle disease viruses. Of poultry, chickens are the most susceptible, ducks and geese are the least. Inapparent infections and carrier states can occur in psittacine and some wild bird populations.

Geographic distribution

Exotic Newcastle disease is endemic in many parts of the world including countries in Asia, the Middle East, Africa, and Central and South America. Some countries in Europe are free of the disease. The United States and Canada have seen high mortality in wild cormorants caused by END. There was an outbreak of END in the US in 2003 in southern California.

Transmission

Transmission can occur by direct contact with feces and respiratory discharges or by contamination of the environment including food, water, equipment, and human clothing. Newcastle disease viruses can survive for long periods in the environment, especially in feces. Generally, virus is shed during the incubation period and for a short time during recovery. Some psittacine species can shed the virus intermittently for a year or more. Virus is present in all parts of the carcass of an infected bird.

Incubation period

The incubation period for Newcastle disease can vary from 2–15 days depending on the severity of the strain and the susceptibility of the population. In chickens with the velogenic form, an incubation period of 2–6 days is common.

Clinical signs

Newcastle disease virus strains used to be grouped into pathotypes based on their clinical signs and virulence. These pathotypes included: asymptomatic enteric, which is generally subclinical; lentogenic or respiratory, which has mild or subclinical respiratory signs; mesogenic, which has respiratory and occasional neurologic signs with low mortality; and velogenic, which is the most virulent pathotype with high mortality rates. The velogenic pathotype is divided into a neurotropic form, which has respiratory and neurologic signs, and a viscerotropic form with hemorrhagic intestinal lesions. This classification is not always that clear–cut and many strains have varied manifestations in different birds. In addition, less pathogenic strains can produce severe clinical signs depending on secondary infections or environmental factors.

The OIE provides a clearer definition for the reporting of any case of Exotic Newcastle as: "Newcastle disease is defined as an infection of birds caused by a virus of avian paramyxovirus serotype 1 (APMV–1) that meets one of the following criteria for virulence:

a. The virus has an intracerebral pathogenicity index (ICPI) in day–old chicks (Gallus gallus) of 0.7 or greater.

Or,

b. Multiple basic amino acids have been demonstrated in the virus (either directly or by deduction) at the C–terminus of the F2 protein and phenylalanine at residue

117, which is the N–terminus of the F1 protein. The term 'multiple basic amino acids' refers to at least three arginine or lysine residues between residues 113 and 116. Failure to demonstrate the characteristic pattern of amino acid residues as described above would require characterization of the isolated virus by an ICPI test."

More specific clinical signs that can be seen with END, particularly in chicken flocks, include an initial drop in egg production followed by numerous deaths within 24–43 hours. Deaths in the flock may continue for 7–10 days. Birds that survive for 12–14 days usually live but may have permanent neurological damage including paralysis, and reproductive damage causing decreased egg production. Viscerotropic strains may cause edema of the head, especially around the eyes, and greenish–dark watery diarrhea. Respiratory and neurological signs can also be seen, though these are not as severe as with the neurotropic form. The neurotropic strains cause respiratory signs of gasping and coughing followed by neurological signs which may include muscle tremors, drooping wings, dragging legs, twisting of the head and neck, circling, depression, inappetence, or complete paralysis. There is generally no diarrhea with the neurotropic form. Clinical signs associated with the various strains can be different in species other than chickens. Psittacines and pigeons may show neurologic signs when infected with the viscerotropic strain. Finches and canaries may show no signs of disease at all. Vaccinated birds will have less severe signs.

Post mortem lesions

There are no specific diagnostic post mortem lesions seen with Newcastle disease. A tentative diagnosis can be made with the examination of several carcasses. Gross lesions can be very similar to highly pathogenic avian influenza; therefore, laboratory isolation and identification is important in definitive diagnosis. Lesions may include edema of the interstitial tissue of the neck, especially near the thoracic inlet, and congestion and sometimes hemorrhages on the tracheal mucosa. Petechiae and small ecchymoses may be found on the mucosa of the proventriculus, especially around the orifices of the mucous glands. Additional lesions may include edema, hemorrhages, necrosis, or ulcerations of lymphoid tissue in the intestinal wall mucosa (including Peyer's patches), as well as edema, hemorrhages, or degeneration of the ovaries.

Morbidity and Mortality

Morbidity and mortality rates can vary greatly depending on the virulence of the virus strain and susceptibility of the host. Environmental conditions, secondary infections, vaccination history, and host species all affect these rates. In chickens, morbidity can be up to 100% with 90% mortality. In other species such as finches and canaries, clinical signs may not be present.

Diagnosis

Clinical

Newcastle disease may be suspected, especially in chicken flocks, with a sudden decrease in egg production, high morbidity and mortality, and the characteristic signs and gross lesions; however, due to the wide variety of signs and similarities to other avian diseases, particularly fowl cholera and highly pathogenic avian influenza, definitive diagnosis requires virus isolation and identification in the laboratory.

Differential diagnosis

Differentials include fowl cholera, highly pathogenic avian influenza, laryngotracheitis, coryza, fowl pox (diphtheritic form), psittacosis (chlamydiosis in psittacine birds), mycoplasmosis, infectious bronchitis, Pacheco's disease (seen in psittacine birds), as well as management problems such as deprivation of water, feed or poor ventilation.

Laboratory tests

Samples for virus isolation are inoculated into 9–11 day old embryonated chicken eggs. Chorioallantoic fluid of dead embryos can then be tested for hemagglutination activity and hemaglutination–inhibition. Further tests may be performed to determine pathogenicity and virus strain. Tests available for serology include hemagglutination–inhibition and enzyme–linked immunosorbent assay (ELISA). Vaccination and previous exposure to disease may affect serology results.

Samples to collect

Before collecting or sending any samples from animals with a suspected foreign animal disease, the proper authorities should be contacted. Samples should only be sent under secure conditions and to authorized laboratories to prevent the spread of the disease. Newcastle disease is zoonotic; samples should be collected and handled with all appropriate precautions.

Swabs can be taken for virus isolation from the trachea and cloaca of live birds, or tissue samples from dead birds including trachea, lung, spleen, cloaca and brain. Feces can also be used for culture. Cell culture broth such as brain and heart infusion broth with high levels of antibiotics should be used for transport. Samples may be pooled in one broth tube if multiple animals are to be tested. Culture tubes should be kept on ice if they will reach the laboratory within 24 hours; otherwise the samples should be quick–frozen and not allowed to thaw during transport. Clotted blood or serum samples can be submitted for serology.

Recommended actions if Newcastle Disease is suspected

Notification of authorities

State and federal veterinarians should be immediately informed of any suspected cases of Newcastle disease. Federal: Area Veterinarians in Charge (AVICS) http://www.aphis.usda.gov/vs/area_offices.htm

State vets: http://www.aphis.usda.gov/vs/sregs/official.html

Quarantine and Disinfection

Recommendations for the control and eradication of Newcastle disease include strict quarantine, slaughter and disposal of all infected and exposed birds, and disinfection of the premises. The reintroduction of new birds should be delayed for 30 days. Pests such as insects and mice should be controlled, human traffic should be limited, and the introduction of new animals with unknown health status should be avoided. Vaccines are available, though they may interfere with testing. Effective disinfectants include the cresylics and phenolics.

Public health

People can be infected with velogenic Newcastle disease and have signs of conjunctivitis which resolve quickly, with virus shed in the ocular discharges for 4–7 days. Infected individuals should avoid direct and indirect contact with avian species during this time. Laboratory workers and vaccination crews are most at risk, with poultry workers rarely being infected. No known infections have occurred from handling or consuming poultry products.

For More Information

World Organization for Animal Health (OIE)

http://www.oie.int

OIE Manual of Standards

http://www.oie.int/eng/normes/mmanual/a_summry.htm

OIE International Animal Health Code

http://www.oie.int/eng/normes/mcode/A_summry.htm

USAHA Foreign Animal Diseases book

http://www.vet.uga.edu/vpp/gray_book/FAD/

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"Newcastle Disease." 30 Aug. 2000 World Organization for Animal Health16 Oct. 2001 <http://www.oie.int/eng/maladies/fiches/a_A060.htm >

Rift Valley Fever

Infectious enzootic hepatitis of sheep and cattle

Last Updated: Jan. 2004

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Etiology

Rift Valley fever results from infection by the Rift Valley fever virus, an RNA virus in the genus Phlebovirus (family Bunyaviridae).

Geographic Distribution

Rift Valley fever is found throughout most of Africa. Outbreaks occur at irregular intervals in southern and eastern Africa, as well as in Egypt, Saudi Arabia and Yemen.

Transmission

Rift Valley fever is transmitted by mosquitoes and is usually amplified in ruminant hosts. The virus appears to survive in the dried eggs of *Aedes* mosquitoes; when these mosquitoes hatch during wet years, epidemics can occur. *Aedes* and other species of mosquitoes can transmit infections from the amplifying hosts. Ticks and biting midges may also be able to spread the virus. Humans do not seem to be infected by contact with live hosts, but can be infected by aerosols or direct contact with tissues during parturition, necropsy, slaughter, laboratory procedures or meat preparation for cooking. The Rift Valley fever virus can be found in raw milk. It is also likely to be present in semen; therefore, sexual transmission may be possible.

Under optimal conditions, the Rift Valley fever virus remains viable in aerosols for more than an hour at 25o C. In a neutral or alkaline pH, mixed with serum or other proteins, the virus can survive for as long as 4 months at 4o C and 8 years below 0o C. It is quickly destroyed in decomposing carcasses by pH changes.

Disinfection

The Rift Valley fever virus is susceptible to low pH, lipid solvents and detergents, ether, chloroform and solutions of sodium or calcium hypochlorite with a residual chlorine content greater than 5000 ppm.

Infections in Humans

Incubation Period

In humans, the incubation period is 2 to 6 days.

Clinical Signs

Infection with the Rift Valley fever virus usually results in an asymptomatic infection or a relatively mild illness with fever and liver abnormalities. The symptoms of uncomplicated infections may include fever, headache, generalized weakness, dizziness, weight loss, myalgia and back pain. Some patients also have stiffness of the neck, photophobia and vomiting. Most people recover spontaneously within 2 days to a week.

Complications - hemorrhagic fever, meningoencephalitis or ocular disease - occur in a small percentage of patients. Hemorrhagic fever usually develops 2 to 4 days after the initial symptoms. The symptoms may include jaundice, hematemesis, melena, a purpuric rash, petechiae and bleeding from the gums. Hemorrhagic fever may progress to frank hemorrhages, shock and death.

Ocular disease and meningoencephalitis are usually seen one to three weeks after the initial symptoms. The ocular form is characterized by retinal lesions and may result in some degree of permanent visual impairment. Death is rare in cases of ocular disease or meningoencephalitis.

Communicability

Virus titers in infected humans are high enough to infect mosquitoes and introduce Rift Valley fever into new areas. Virus can be found in the blood and tissues.

Diagnostic Tests

The Rift Valley fever virus can be isolated from the blood, brain, liver or other tissues; in living hosts, viremia is usually seen only during the first three days of fever. The virus can be grown in numerous cell lines including baby hamster kidney cells,

monkey kidney (Vero) cells, chicken embryo reticulum, and primary cultures from cattle or sheep. Hamsters, adult or suckling mice, embryonated chicken eggs or 2-day–old lambs can also be used.

Virus antigens can be detected in blood and tissue samples by various tests including reverse transcription polymerase chain reaction (RT-PCR) testing. Enzyme-linked immunoassay (ELISA) and other serologic assays can detect specific IgM or rising titers.

Treatment and Vaccination

No specific treatment, other than supportive care, is available; however, ribavirin has been promising in animal studies. Interferon, immune modulators and convalescent-phase plasma may also prove to be helpful. Most cases of Rift Valley fever are relatively brief and mild illnesses and may not require treatment.

A human vaccine has been developed and other vaccines are in earlier stages of investigation. None of these vaccines are sold commercially, but one may be available from government sources for people who are occupationally exposed.

Morbidity and Mortality

Humans are highly susceptible to Rift Valley fever. Most cases develop in veterinarians, abattoir workers and others who work closely with blood and tissue samples of animals. During outbreaks in animals, mosquitoes may spread the virus to humans and cause epidemics. In Egypt, approximately 200,000 human cases and 598 deaths occurred during a 1977 epidemic.

Most people with Rift Valley fever recover spontaneously within a week. Ocular disease is seen in approximately 0.5 to 2% and meningoencephalitis and haemorrhagic fever in less than 1%. The case fatality rate for hemorrhagic fever is about 50%. Deaths rarely occur in cases of eye disease or meningoencephalitis but 1 to 10% of patients with ocular disease have some permanent visual impairment. The overall case fatality rate for all patients with Rift Valley fever is less than 1%.

Infections in Animals

Species Affected

Rift Valley fever can affect many species, including sheep, cattle, goats, buffalo, camels, monkeys, gray squirrels and other rodents. The primary amplifying hosts are sheep and cattle. Viremia without severe disease may be seen in adult cats, dogs, horses and some monkeys, but severe disease can occur in newborn puppies and kittens. Rabbits, pigs, guinea pigs, chickens and hedgehogs do not become viremic.

Incubation Period

The incubation period can be as long as 3 days in sheep, cattle, goats and dogs. In newborn lambs, it is 12 to 36 hours. Experimental infections usually become evident after 12 hours in newborn lambs, calves, kids and puppies.

Clinical Signs

The clinical signs vary with the age, species and breed of the animal. In endemic regions, epidemics of Rift Valley fever can be recognized by the high mortality in newborn animals and abortions in adults.

Rift Valley fever is usually most severe in young animals. In young lambs, a biphasic fever, anorexia and lymphadenopathy may be followed by weakness and death within 36 hours; hemorrhagic diarrhea or abdominal pain can also occur. The mortality rate may reach 90 to 100% in neonates. Disease is similar in young calves: fever, anorexia and depression are typical, with mortality rates of 10 to 70%.

The symptoms in adult sheep may include fever, a mucopurulent nasal discharge (sometimes bloodstained), hemorrhagic or foul-smelling diarrhea, vomiting, jaundice, abortion and an unsteady gait. In adult cattle, fever, anorexia, weakness, excessive salivation, fetid diarrhea, abortion and decreased milk production may be seen. In some cases, abortion can be the only sign of infection in these two species. Similar but milder infections occur in goats. Adult camels do not develop symptoms other than abortion but young animals may have more severe disease.

Communicability

Infections are typically transmitted by mosquitoes and not by direct contact; however, during parturition, necropsy or slaughter, viruses in the tissues can be spread by aerosols and enter the skin through abrasions. The Rift Valley fever virus has also been found in raw milk and may be present in semen.

Diagnostic Tests

Rift Valley fever can be diagnosed by virus isolation. The virus can be isolated from the blood of febrile animals. It can also be recovered from the tissues from dead animals and aborted fetuses; the liver, spleen and brain are generally used. Virus can be grown in numerous cell lines including baby hamster kidney cells, monkey kidney (Vero) cells, chicken embryo reticulum and primary cultures from cattle or sheep. Hamsters, adult or suckling mice, embryonated chicken eggs or 2-day-old lambs can also be used.

Virus titers in tissues are often high; a rapid diagnosis can sometimes be made with complement fixation, neutralization and agar gel diffusion tests on tissue suspensions. Rapid tests may need to be confirmed by virus isolation. Virus antigens can also be detected by immunofluorescent staining of the liver, spleen or brain. Enzyme

immunoassays and immunodiffusion tests can identify virus in the blood.

Serologic tests are helpful in epidemiologic studies but may be of limited use in diagnosis. Available tests include virus neutralization, enzyme-linked immunosorbent assay (ELISA), hemagglutination inhibition, immunofluorescence, complement fixation and immunodiffusion assays. Cross-reactions may occur with other phleboviruses.

Treatment and Vaccination

The only treatment is supportive care. Vaccines are available in some countries.

Morbidity and Mortality

Epidemics of Rift Valley fever tend to occur at intervals, when heavy rainfalls cause infected mosquitoes to hatch and a susceptible animal population has developed. Outbreaks are characterized by large numbers of abortions and high mortality in neonates. Indigenous cattle may have asymptomatic infections, while more severe disease is seen in exotic species.

The mortality rate can be very high in young animals, with fatalities decreasing in older age groups. Deaths are common in neonatal lambs, calves, kids, puppies and kittens. The mortality rate is 90 to 100% in newborn lambs, 40 to 60% in weaners and 15 to 30% in adult sheep. Ewes that abort are more likely to have a fatal infection. In calves, mortality rates range from 10 to 70%. Fewer than 10% of infections in adult cattle are fatal. Abortion rates range from 5 to almost 100% in ewes but are usually less than 10% in cattle.

Post-Mortem Lesions

The most consistent lesion is hepatic necrosis; the necrosis is more extensive and severe in younger animals. In aborted fetuses and newborn lambs, the liver may be very large, yellowish-brown to dark reddish-brown, soft and friable, with patchy congestion. Multiple gray to white necrotic foci are usually present, but may only be visible microscopically. The liver lesions are usually less severe in adult animals and may consist of numerous pinpoint necrotic foci.

Additional lesions may include jaundice, widespread cutaneous hemorrhages and fluid in the body cavities. The peripheral lymph nodes and spleen may be enlarged and edematous and often contain petechiae. The walls of the gallbladder are often edematous, with visible hemorrhages. A variable degree of inflammation or hemorrhagic enteritis can sometimes be found in the intestines. In lambs, many small hemorrhages are usually seen in the abomasal mucosa and the small intestine and abomasum may contain dark chocolate-brown contents, with partially digested blood. In addition, petechial and ecchymotic hemorrhages may be seen on the surface of other internal organs.

Internet Resources

Animal Health Australia.

The National Animal Health Information System (NAHIS)

http://www.brs.gov.au/usr-bin/aphb/ahsq?dislist=alpha

CDC Rift Valley fever page

http://www.cdc.gov/ncidod/dvrd/spb/mnpages/dispages/rvf.htm

Manual for the Recognition of Exotic Diseases of Livestock

http://panis.spc.int/

Medical Microbiology

http://www.gsbs.utmb.edu/microbook

Office International des Epizooties (OIE)

Manual of Standards for Diagnostic Tests and Vaccines

http://www.oie.int/eng/normes/mmanual/a_summry.htm

The Merck Veterinary Manual

http://www.merckvetmanual.com/mvm/index.jsp

WHO Fact Sheet on Rift Valley fever

http://www.who.int/inf-fs/en/fact207.html

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Mebus, C.A. "Rift Valley Fever." In *Foreign Animal Diseases*. Richmond, VA: United States Animal Health Association, 1998, pp. 353-61. 16 Nov 2002 <http://www.vet.uga.edu/vpp/gray_book/FAD/RVF.htm>.

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"Rift Valley Fever." In *Manual for the Recognition of Exotic Diseases of Livestock: A Reference Guide for Animal Health Staff*. Food and Agriculture Organization of the United Nations, 1998. 27 November 2002 <http://panis.spc.int/RefStuff/Manual/Multiple%20Species/RIFTVALLEY%20FEVER.HTML>.

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Swine Vesicular Disease

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Importance

Swine vesicular disease (SVD) has almost identical clinical signs to foot–and–mouth disease, but is only seen in pigs. Neither disease is present in North America. Differentiation of these two vesicular diseases is important, as the introduction of foot–and–mouth disease could cause severe economic losses.

Etiology

Swine vesicular disease virus (SVDV) is a porcine enterovirus in the family Picornaviridae. It is antigenically related to the human enterovirus Coxsackie B–5 and unrelated to other known porcine enteroviruses.

Species affected

Pigs are the only species that are naturally infected. Humans have been infected while working in a laboratory setting. Baby mice can be experimentally infected.

Geographic distribution

While SVD has been seen in Italy, England, Scotland, Wales, Malta, Austria, Belgium, France, the Netherlands, Germany, Poland, Switzerland, Greece, and Spain, the disease has been eradicated from all European countries. SVD still remains in many countries in the Far East.

Transmission

Transmission can occur by ingestion of contaminated meat scraps and contact with infected animals or infected feces. Pigs can excrete the virus from the nose, mouth, and feces up to 48 hours before clinical signs are seen. Virus can be shed in the feces for up to 3 months following infection.

SVDV can survive for long periods of time in the environment. This virus is resistant to heat up to 157°F (69°C) and pH ranging from 2.5–12. It can also survive up to 2 years in lymphoid tissue contained in dried, salted, or smoked meat.

Incubation period

The incubation period is 2–7 days following exposure to infected pigs and 2–3 days after the ingestion of contaminated feed.

Clinical signs

The clinical signs of swine vesicular disease are very similar to foot–and–mouth disease, and include fever, salivation, and lameness. Vesicles and erosions can be seen on the snout, mammary glands, coronary band, and interdigital areas. Vesicles in the oral cavity are relatively rare. The infection may be subclinical, mild, or severe depending on the virulence of the strain. Severe signs are generally seen only in pigs housed on damp concrete. Younger animals can be more severely affected. Neurological signs due to encephalitis are rare. These include shivering, unsteady gait, and chorea (rhythmic jerking) of the legs. Abortion is not typically seen. Recovery occurs within 2–3 weeks with little permanent damage.

Post mortem lesions

The only post–mortem lesions are the vesicles that can be seen in live pigs. These lesions are similar to those of other vesicular diseases, including foot–and–mouth disease.

Morbidity and Mortality

Swine vesicular disease is considered to be moderately contagious. Compared to foot–and–mouth disease, morbidity is lower and the lesions are less severe. Mortality is not generally a concern with swine vesicular disease.

Diagnosis

Clinical

Swine vesicular disease or other vesicular diseases should be suspected when vesicles or erosions are found on the mouth and/or feet of pigs. In swine vesicular dis-

ease outbreaks, pigs will be the only species affected, the lesions will be mild, and there will be no mortality. Other vesicular diseases must be ruled out with laboratory tests.

Differential diagnosis

Differentials for swine vesicular disease include foot–and–mouth disease, vesicular stomatitis, vesicular exanthema of swine, and chemical or thermal burns.

Laboratory tests

SVDV can be identified using enzyme–linked immunosorbent assay (ELISA), the direct complement fixation test, and virus isolation in pig–derived cell cultures. Virus neutralization and ELISA can be used for serological diagnosis.

Samples to collect

Before collecting or sending any samples from vesicular disease suspects, the proper authorities should be contacted. Samples should only be sent under secure conditions and to authorized laboratories to prevent spread of the disease. Since vesicular diseases can not be distinguished clinically, and some are zoonotic, samples should be collected and handled with all appropriate precautions. Samples include vesicular fluid, the epithelium covering vesicles, esophageal–pharyngeal fluid, unclotted whole blood collected from febrile animals, and fecal and serum samples from infected and non–infected animals.

Recommended actions if swine vesicular disease is suspected

Notification of authorities

State and federal veterinarians should be immediately informed of any suspected vesicular disease. Federal: Area Veterinarians in Charge (AVICS) http://www.aphis.usda.gov/vs/area_offices.htm

State vets: http://www.aphis.usda.gov/vs/sregs/official.html

Quarantine and Disinfection

Infected farms or areas should be quarantined. Infected pigs and those in contact with them should be slaughtered and disposed of. The premises should be thoroughly cleaned and disinfected. In the presence of organic matter, sodium hydroxide (1% combined with detergent) can be used. Oxidizing agents and iodophors used with detergents work well for personal disinfection in the absence of gross organic matter.

Public health

Seroconversion and mild clinical disease with one case of meningitis has been seen in laboratory workers.

For More Information

World Organization for Animal Health (OIE)

http://www.oie.int

OIE Manual of Standards

http://www.oie.int/eng/normes/mmanual/a_summry.htm

OIE International Animal Health Code

http://www.oie.int/eng/normes/mcode/A_summry.htm

USAHA Foreign Animal Diseases book

http://www.vet.uga.edu/vpp/gray_book/FAD/

Manual for the Recognition of Exotic Diseases of Livestock

http://www.spc.int/rahs/

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Mebus C.A. "Swine Vesicular Disease." In *Foreign Animal Diseases*. Richmond, VA: United States Animal Health Association, 1998, pp. 392–395.

"Swine Vesicular Disease." In *Manual of Standards for Diagnostic Tests and Vaccines*. Paris: World Organization for Animal Health, 2000, pp. 100–104.

Swine Vesicular Disease. Disease Lists and Cards. World Organization for Animal Health. <http://www.oie.int>.

"Swine Vesicular Disease." In Manual for the Recognition of Exotic Diseases of Livestock: A Reference Guide for Animal Health Staff. Food and Agriculture Organization of the United Nations, 2002. 21 April 2003 <http://www.spc.int/rahs/Manual/Porcine/SVDE.HTM>.

Vesicular Stomatitis

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Importance

Vesicular stomatitis is an important zoonotic vesicular disease found in the Americas. This disease has almost identical clinical signs to foot–and–mouth disease in cattle and pigs. The signs of vesicular stomatitis are also very similar to swine vesicular disease and vesicular exanthema of swine. Differentiation of these vesicular diseases is important. The spread of vesicular stomatitis within the United States could bring restrictions on exports of animals and their products to other countries that do not have the disease.

Etiology

Vesicular stomatitis virus (VSV) is a Vesiculovirus in the family Rhabdoviridae. It is a large bullet-shaped RNA virus. There are two strains of VSV that are considered domestic to the United States: New Jersey and Indiana-1; and there are three other exotic strains in South America: Indiana-2 (Cocal), Indiana-3 (Alagoas) and Piry.

Species affected

Horses, donkeys, mules, cattle, swine, South American camelids, and humans can be affected by VSV. Sheep and goats are resistant and rarely show clinical signs. Experimentally, a wide host range has been found including deer, raccoons, bobcats, and monkeys.

Geographic distribution

Vesicular stomatitis occurs only in some areas in the United States, Mexico, Central America and the northern part of South America.

Transmission

Vesicular stomatitis can be transmitted by insect vectors, especially sand flies (*Lutzomyia shannoni*) and black flies (*Simuliidae*), which have both been shown to have transovarial transmission. It can also be transmitted by contact with infected animals and contaminated objects. Humans may be infected by contact or aerosol.

Incubation period

The incubation period of VSV is usually 3–5 days. Vesicles can occur within 24 hours. The incubation period in humans is 24–48 hours.

Clinical signs

All animal species develop fever. Horses are affected the most severely, with oral and coronary band vesicles leading to signs of drooling, chomping, mouth rubbing, and lameness. The signs in cattle and pigs are very similar to foot–and–mouth disease, with vesicles in the oral cavity, mammary glands, coronary band, and interdigital region. Compared to other vesicular diseases, animals with vesicular stomatitis are more likely to have lesions isolated to only one part of the body, such as the mouth or the feet. Animals recover within two weeks, longer with secondary infection.

Post mortem lesions

Mouth and foot vesicles are seen on post mortem. Heart and rumen lesions seen with foot and mouth disease are not seen with vesicular stomatitis.

Morbidity and Mortality

Morbidity varies with conditions, but can be up to 90%. Infection is typically sporadic in an exposed group. Death is not as common in young animals as with foot and mouth disease. The mortality rate is low.

Diagnosis

Clinical

Diagnosis is similar to that of foot and mouth disease due to the similar clinical signs. Vesicular stomatitis affects horses, but foot and mouth disease does not. In addition, vesicular stomatitis is not as contagious and does not spread as rapidly

through a group of animals. Most VSV-infected animals have lesions in only one area of the body. Heart and rumen lesions typical for foot and mouth disease are not seen in vesicular stomatitis. Animals kept in stables during a vesicular stomatitis outbreak are less likely to contract the disease.

Differential diagnosis

In cattle, differentials include foot and mouth disease, foot rot, and chemical or thermal burns. Oral lesions can be similar to those seen with rinderpest, infectious bovine rhinopneumonitis, bovine virus diarrhea, malignant catarrhal fever, and bluetongue. In pigs, differentials include foot and mouth disease, swine vesicular disease, vesicular exanthema of swine, foot rot, and chemical and thermal burns.

Laboratory tests

VSV can be isolated in tissue culture, or detected by RT-PCR. Viral antigen can be detected using ELISA, complement fixation, or virus neutralization tests. Paired acute and convalescent serum samples may be tested for antibodies using ELISA, virus neutralization, or complement fixation tests.

Samples to collect

Before collecting or sending any samples from vesicular disease suspects, the proper authorities should be contacted. Samples should only be sent under secure conditions and to authorized laboratories to prevent spread of the disease. Since vesicular diseases can not be distinguished clinically, and some are zoonotic, samples should be collected and handled with all appropriate precautions. Samples include vesicular fluid, the epithelium covering vesicles, esophageal–pharyngeal fluid, unclotted whole blood collected from febrile animals, and fecal and serum samples from infected and non-infected animals.

Recommended actions if vesicular stomatitis is suspected

Notification of authorities

State and federal veterinarians should be immediately informed of any suspected vesicular disease. Federal: Area Veterinarians in Charge (AVIC): http://www.aphis.usda.gov/vs/area_offices.htm

State vets: http://www.aphis.usda.gov/vs/sregs/official.html

Quarantine and Disinfection

Isolation of animals showing clinical signs helps control the spread of vesicular stomatitis within a herd. There should be no movement of animals from an infected property for at least 30 days after all lesions are healed. Insect control may help prevent disease spread. Disinfectants include 2% sodium carbonate, 4% sodium hydroxide, 2% iodophore disinfectants, and chlorine dioxide.

Public health

Vesicular stomatitis occurs often in humans as an influenza-like illness rarely causing vesicles. Infected humans develop fever, headache, muscular aches, and, rarely, oral blisters similar to herpes virus. Recovery usually occurs within 4–7 days.

For More Information

World Organization for Animal Health (OIE)

http://www.oie.int

OIE Manual of Standards

http://www.oie.int/eng/normes/mmanual/a_summry.htm

OIE International Animal Health Code

http://www.oie.int/eng/normes/mcode/A_summry.htm

USAHA Foreign Animal Diseases book

http://www.vet.uga.edu/vpp/gray_book/FAD/

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Section 3

Additional Resources

TO: Practicing Veterinarians

FROM: State Veterinarian's Office

This protocol for investigation of a foreign animal disease (FAD) gives the emergency response contact numbers that can be used for all reportable diseases (including anthrax).

Missouri Emergency Response Protocol for Reporting a Foreign Animal Disease

Emergency Response Plan: This plan is for dealing with all foreign animal diseases, including foot-and-mouth disease. The goal of this plan is to detect, control, and eradicate all intentional (agroterrorism) or accidental introduction of the disease. This plan considers presumptive positive cases and confirmed positive cases of any foreign animal disease.

I. Foreign Animal Diseases, including vesicular diseases in cloven-hoofed animals, will be handled as an animal disease emergency. Any practicing veterinarian that suspects a foreign animal disease, including foot-and-mouth disease (FMD), will notify the State Veterinarian's Office at (573) 751-3377 or cell phones (573) 578-8837, (573) 690-2831, and (573) 694-7515 or contact the State Emergency Management Agency (SEMA) 24-hour duty officer at (573) 751-2748.

II. Any case with an animal exhibiting clinical signs consistent with a foreign animal disease will be reported to the office of the State Veterinarian and/or the USDA Area Veterinarian In Charge (AVIC). The State Veterinarian will immediately dispatch a Foreign Animal Disease Diagnostician (FADD) to the premises. If the reporting veterinarian, based on clinical experience and reasonable judgment, determines that the disease is highly suspicious of an FAD, the State Veterinarian or APHIS Area Veterinarian in Charge may authorize an interim quarantine of the premises by telephone to the reporting veterinarian. The FADD will assess the situation upon arrival at the premises and may confirm the quarantine of the premises should the situation warrant such action in his/her opinion. The FADD will also collect appropriate samples for laboratory analysis. Any veterinarian reporting such an incident must remain on the premises until released by the FADD. The samples will be examined immediately and with the highest priority. Samples will be submitted to the laboratory within
24 hours after the beginning of the investigation. The FADD will use clinical signs, history, and professional experience to assess the risk of the disease. Categories of risk will be assigned as (1) Unlikely, (2) Possible, or (3) Highly Likely.

"Unlikely" or "Possible" Risk

(1) An official state quarantine will be issued until the laboratory result rules out the foreign animal disease.

(2) If the laboratory test is negative the animals will be released from quarantine.

"Highly Likely" Risk

(1) FADD will immediately contact and consult with the AVIC and State Veterinarian.

(2) The submitted samples will be given the highest priority to reach a diagnosis within 24 hours.

(3) A quarantine will be placed on the farm of the index herd.

(4) The FADD will work with the producer on appropriate biosecurity and public health measures.

(5) A movement control zone quarantine of six miles will be placed around the index farm.

(6) Producers on adjacent farms will be notified of the movement control zone quarantine by other regulatory personnel (not the FADD).

The State Veterinarian will take the following actions:

(1) Notify Director, Missouri Department of Agriculture, of the suspicious case.

(2) Consider stopping movement of all animals within the state.

(3) Notify all field veterinarians, State Emergency Management Agency (SEMA), Food Safety and Inspection Service (FSIS), University Extension, and livestock industry partners.

(4) Prepare a press release and notify the Missouri Veterinary Medical Association.

III. A presumptive positive case (animal with clinical signs and initial laboratory positive test for the agent) will initiate the following actions:

(1) State Veterinarian and AVIC will:

- Stop all movement of susceptible species of livestock in the state for 72 hours.
- Initiate depopulation and disposal of infected herd(s). Identified burial sites will be selected to minimize negative environmental impact.
- Provide information to the Missouri Department of Natural Resources on the plan to dispose of dead animals.
- Keep accurate records of depopulated animals for possible indemnity payments at a later time.
- Coordinate with SEMA to achieve Governor's Declaration of Emergency.
- Continue quarantine and movement restrictions.
- Continue active epidemiological investigation and surveillance to detect new cases.
- If appropriate, make decision on use of foot-and-mouth disease (FMD) vaccine to control disease.

(2) SEMA Director will:

- Activate State Emergency Response Plan.
- Assist with coordination of movement control within the State.
- Coordinate with FEMA on Federal Emergency Response Plan Activation.

(3) USDA, APHIS will:

- Activate the National Incident Management System (NIMS).
- Coordinate with other federal agencies on emergency declaration.
- Impose a federal quarantine on the state for interstate commerce.
- Cooperate with the State Veterinarian in identification of a source of infection.
- Coordinate national surveillance.

Reportable Diseases and Follow-Up Guidelines

I. Animal and Livestock Diseases

Reportable Communicable Diseases

The following are diseases that must be reported to state (573) 751-3377 or federal (573) 636-3116 agriculture officials within 24 hours of suspicion or diagnosis:

Avian

- Avian infectious encephalomyelitis
- Avian influenza
- Fowl typhoid (salmonella gallinarum)
- Infectious laryngotracheitis
- Mycoplasma gallisepticum (MG)
- Mycoplasma meleagridis (MM)
- Mycoplasma synoviae (MS)
- Paramyxovirus infection (other than Newcastle Disease)
- Psittacosis (chlamydiosis and ornithosis)
- Pullorum disease (salmonella pullorum)
- Salmonellosis caused by Salmonella enteritidis
- Velogenic viscerotropic Newcastle disease

Bovine

- Akabane
- Anthrax
- Bluetongue
- Bovine babesiosis (Texas fever, piroplasmosis)
- Bovine spongiform encephalopathy (BSE)
- Brucellosis
- Contagious bovine pleuropneumonia
- East Coast fever (coastal fever, theileriosis)
- Ephemeral fever (three-day sickness)
- Foot-and-mouth disease
- Gonderiosis (theileriosis)
- Heartwater
- Hemorrhagic septicemia (Asiatic type 1 shipping fever)
- Ibaraki
- Infectious petechial fever
- Louping Ill
- Lumpy skin disease (pseudourticaria)
- Malignant catarrhal fever
- Paratuberculosis
- Pseudorabies
- Q fever
- Rift Valley fever
- Rinderpest (cattle plague)
- Scabies
- Screwworm
- Sweating sickness (tick-borne toxicosis)
- Tuberculosis
- Trypanosomiasis (nagana)
- Vesicular stomatitis
- Wesselborne disease

Caprine-Ovine

- Bluetongue
- Borna disease
- Brucellosis caused by Brucella meletensis and B. ovis
- Caseous lymphadenitis
- Contagious agalactia of sheep and goats
- Contagious caprine pleuropneumonia
- Foot-and-mouth disease
- Goat and sheep pox
- Gonderiosis (theileriosis)
- Heartwater
- Nairobi sheep disease
- Peste des petits ruminants (kata)
- Screwworm
- Tuberculosis
- Rift Valley fever
- Scabies
- Scrapie
- Vesicular stomatitis
- Visna-Maedi (chronic progressive pneumonia)

Equine

- African Horse sickness
- Babesiosis (piroplasmosis)
- Contagious equine metritis
- Dourine (equine trypanosomiasis)
- Eastern equine encephalomyelitis
- Epizootic lymphangitis
- Equine infectious anemia (EIA)
- Equine piroplasmosis
- Equine rhinopneumonitis
- Equine viral arteritis
- Glanders
- Potomac horse fever
- Venezuelan equine encephalomyelitis
- Vesicular stomatitis
- Western equine encephalomyelitis

All Species

- Anthrax
- Brucellosis
- Exotic myiasis
- Foot-and-mouth disease
- Paratuberculosis (Johnes disease)
- Rabies
- Tuberculosis
- Vesicular exanthema
- Vesicular stomatitis

Porcine

- African swine fever
- Brucellosis
- Foot-and-mouth disease
- Hog cholera
- Porcine babesiosis
- Pseudorabies
- Swine vesicular disease
- Teschen disease (porcine encephalomyelitis)
- Vesicular exanthema
- Vesicular stomatitis

Cervidae

- Chronic Wasting Disease (CWD)

II. Communicable Diseases

The following must be reported to the local public health agency or the Missouri Department of Health and Senior Services during business hours at (573) 751-9071 or after hours/weekends at 800-392-0272 within 24 hours of suspicion or diagnosis:

- Rabies, animal or human

III. Disease From Potential Agents of Bioterrorism:

These diseases are divided into three categories of decreasing priority. Some are considered to be “foreign animal diseases” (e.g., Venezuelan equine encephalomyelitis), and most are zoonotic. A number of these diseases are reportable to state or federal agriculture officials, as noted above. All diseases (animal or human) suspected to have resulted from an act of bioterrorism must be reported immediately to (1) state (573) 751-3377 or federal (573) 636-3116 agriculture officials and/or (2) the Missouri Department of Health and Senior Services (business hours: 573-751-9071; after hours/weekends: 800-392-0272).

Category A

- Anthrax (Bacillus anthracis)
- Botulism (Clostridium botulinum toxin)
- Plague (Yersinia pestis)
- Smallpox (Variola major)
- Tularemia (Francisella tularensis)
- Viral Hemorrhagic Fevers (Ebola, Marburg, Lassa, Machupo)

Category B

- Brucellosis (Brucella species)
- Glanders (Burkholderia mallei)
- Melioidosis (Burkholderia pseudomallei)
- Psittacosis (Chlamydophila psittaci)
- Q Fever (Coxiella burnetii)

- Typhus Fever (Rickettsia prowazekii)
- Viral Encephalitis (VEE, EEE, WEE)
- Toxins (Ricinus communis, Clostridium perfringens, Staphylococcus aureus)

Category C

- Nipah (Nipah virus)
- Hantavirus (Hantavirus)

IV. Recommendations for Veterinarians Examining Animals With Suspected Foreign Animal Disease or Disease Resulting From an Act of Bioterrorism

Veterinarians who examine or treat animals with suspected foreign animal disease (FAD) or disease resulting from an act of bioterrorism (BT) should use infection control precautions to protect the health of themselves, staff, and clients, as well as other animal patients in the area. Generally, animals suspected of having a FAD/BT disease should not be moved from their home premises. If a tentative diagnosis of FAD/BT disease is not made until the animal is brought to a clinic, the animal should be isolated immediately. In either event, veterinarians and staff should wear personal protective equipment (PPE) during the examination. The animal should not be taken to a common treatment room, and all treatments and diagnostics should be performed in the examination room. The number of staff allowed in the exam room and that come in contact with the animal should be limited to as few persons as possible. Veterinarians who do not wish to examine an animal with suspected FAD/BT disease should advise the animal's owner to contact the state agriculture or health department for further guidance.

Infection Control Precautions

The most common routes for transmission of FAD/BT diseases are through direct contact with infected animals and by airborne spread. In addition, all avenues of transmission for some of these agents are not totally understood. When examining animals with suspected FAD/BT disease, veterinarians and staff should use the following precautions:

1. Hand hygiene after all contact with a sick animal and contaminated surfaces.

2. Use of gown and gloves for any contact with the sick animal and contaminated surfaces.

3. Eye protection (e.g., tight-fitting goggles or face shield) if splash or spray of body fluids is likely.

4. Respiratory protection, including a NIOSH-certified N95 filtering disposable respirator (or other respirator offering comparable levels of respiratory protection), for entering the exam room or patient care area. If N95 or comparable respirators are not available, then surgical masks should be worn to protect against transmission through contact or large droplets.

5. Contain and dispose of contaminated waste after consultation with state or local health officials. Do not dispose of waste in landfills or dumps.

6. Handle used patient-care equipment in a manner that prevents contamination of skin and clothing. Ensure that used equipment has been cleaned and reprocessed appropriately.

7. Ensure that procedures are in place for cleaning and disinfecting contaminated environmental surfaces. EPA-registered detergent-disinfectants currently used by healthcare or veterinary facilities for environmental sanitation may be used. Manufacturer's recommendations for dilution (i.e., concentration), contact time, and care in handling should be followed.

8. Handling of laundry (e.g., towels, clothing) should be evaluated on a case-by-case basis. For many agents, laundry may be washed in a standard washing machine with hot water and detergent. The use of chlorine bleach during hot-water washing can provide an added measure of safety. Washing laundry contaminated with a resistant form of an organism (e.g., spore formers) may not be sufficient. The state agriculture or health department may be

consulted for guidance. Care should be used when handling soiled laundry to avoid direct contact with contaminated material. Soiled laundry should not be shaken or otherwise handled in a manner that may aerosolize infectious particles.

V. Risk Communication

In the event of a FAD/BT disease, it is highly advisable not to talk to media or to release information to other individuals or agencies that do not have the "need to know." It is important that information be communicated accurately and in a timely manner to the media, public, and decision-makers, but this is best accomplished by using public information resources available through state and federal agencies. Failure to control the message could result in misinterpretation of data, distortion of events, and information being taken out of context.

General Signs of Reportable Animal and Poultry Diseases

I. Vesicles/erosions on tongue, nose, lips, feet, teats
- ➢ Foot-and-mouth disease
- ➢ Vesicular stomatitis
- ➢ Swine vesicular disease
- ➢ Bluetongue of cattle
- ➢ Sore mouth (contagious ecthyma) of sheep and goats
- ➢ Bovine virus diarrhea
- ➢ Malignant catarrhal fever
- ➢ Vesicular exanthema of swine
- ➢ Rinderpest
- ➢ Contagious foot rot of sheep

II. High herd/flock morbidity, low fatality
- ➢ Foot-and-mouth disease
  - • Cattle, swine, sheep, goats, all cloven hoofed susceptible
  - • Does not occur in horses
  - • 100 percent herd incidence in the U.S.
  - • Less than 1 percent fatality, higher in calves
- ➢ Vesicular stomatitis
  - • Higher morbidity and more severe in horses than cattle or swine
  - • Lower morbidity and severity in cattle and swine than FMD
  - • Sheep and goats rarely infected

III. High herd/flock morbidity, high fatality
- ➢ Hog cholera
- ➢ African swine fever
  - • Eradicated from Western Hemisphere
  - • Virus with lower virulence has emerged
- ➢ Exotic Newcastle disease
- ➢ High pathogenic avian influenza
- ➢ Rift Valley fever (morbidity and fatality variable among outbreaks)
- ➢ Rinderpest

IV. Low morbidity, high fatality
- ➢ Anthrax
- ➢ Scrapie
- ➢ Bovine spongiform encephalopathy
- ➢ Chronic wasting disease

V. Abortion storms not associated with known pathogens for the location
- ➢ Rift Valley fever, early sign in sheep and cattle, may be sentinels for impending human disease
- ➢ Q fever, abortions of sheep, goats and cattle, late pregnancy, usually the only sign in animals, shorter incubation than disease in humans so may precede human disease
- ➢ Brucella abortus in cattle (always remain vigilant!)

VI. Unusual respiratory sounds in a poultry house
- ➢ Avian influenza
- ➢ Exotic Newcastle disease

VII. Acute onset, rapid infection
- ➢ Foot-and-mouth disease
- ➢ Hog cholera
- ➢ Rift Valley fever
- ➢ African swine fever
- ➢ Swine vesicular disease
- ➢ Rinderpest

VIII. Central nervous system signs
- ➢ Viral encephalidities (eastern, western, Venezuelan, West Nile)
- ➢ Hog cholera
- ➢ Scrapie
- ➢ Bovine spongiform encephalopathy
- ➢ Botulism

IX. Fly larvae (maggots) in living tissue
- ➢ Screwworms

X. Sudden death without clinical signs
- ➢ Anthrax
- ➢ Rinderpest

Missouri Veterinary Medical Association
Emergency Management and Public Health Committee

Biosecurity of Veterinary Practices

Practitioners, their staffs and technicians must be aware of the clinical signs of the important foreign animal diseases so that they are able to suspect a potentially dangerous disease seen on a farm call, in the clinic or by client description over the telephone. Education of veterinarians and staffs should focus on vesicular diseases, all of which are reportable, hog cholera, which might look like any other highly contagious and deadly swine disease, highly contagious poultry diseases and anthrax.

Clinic and Hospital Biosecurity

- Carefully screen new employees; double check education and employment histories.
- Be aware of repeated visits by strangers and unrecognized vehicles in the vicinity.
- Build a perimeter fence; possibly install a security system
- Limit internal traffic between large animal and small animal facilities; place disinfectant tubs with boot brushes for use between facilities.
- Carefully screen unknown visitors, prohibit entry to animal facilities and be aware of animal extremist organizations.
- Livestock arriving at the large animal facility should be observed for signs of obvious abnormalities before unloading.
- Emergency contact phone numbers should be posted in the clinic and carried in practice vehicles. A wallet-size card with these contact numbers was mailed to all veterinarians in Missouri by the MVMA.

Vehicle and Livestock Facility Biosecurity

- Wear clean outer clothing and disinfect boots when entering and leaving livestock facilities. Livestock producers expect this level of biosecurity.
- Carry Virkon-S disinfectant, boot tub and brush, clean coveralls, disposable nitrile gloves, surgical masks and caps, and a two-gallon garden sprayer for external disinfection of the vehicle if necessary.
- Boots must be brushed clean with disinfectant. It is very difficult to sterilize fecal material.
- When entering a premises where vesicular or other highly contagious disease is suspected, wear disposable coveralls and plastic overboots which can be left at the facility for burning or other disposal.
- Elasta-A-Boots are tough quality plastic disposable boots, about $0.50 a pair, and Disposable Coveralls, about $1.25 a pair, are available from Nasco and other farm supply outlets. These items should be routine equipment in vehicles and clinics.
- If a reportable disease is suspected it is best to park the practice vehicle at the farm perimeter.
- If a reportable disease is suspected, state authorities must be contacted immediately beginning with the State Veterinarian, followed by others in order as listed in "Contacts for Animal Emergencies" if necessary. The first contact should always be the Office of the State Veterinarian.
- After reporting the disease, the veterinarian should remain on the farm until the arrival of the Foreign Animal Disease Diagnostician (FADD)..
- Contaminated clothing should be placed in a heavy plastic bag and washed in hot water with mild bleach. Plastic coveralls and boots left at the suspect farm for burning or other disposal.
- Veterinarians should emphasize farm biosecurity to clients.

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Suggestions to Protect Your Livestock Operation

Restrict human traffic to farmstead

- Have a secure perimeter fence, limit entry to one gate.
- Post a sign forbidding entry without permission. Have visitors sign a register.
- Be aware of repeat sightings of unknown persons and vehicles near the farm
- Supply a tub of disinfectant, freshen daily, and a brush for scrubbing footwear.
- Provide plastic over-boots for visitors.
- Footwear worn away from the farmstead to any place where livestock are present should be scrubbed and disinfected before reentering the farm.

Restrict vehicle entry to farmstead

- Stop all nonessential vehicles from entering the farm and arrange whenever possible for collection and delivery of supplies to take place at farm boundary.
- If a vehicle must enter the farmstead make sure that prior to entry their wheels are sprayed with disinfectant.
- Livestock haulers should clean, disinfect and let dry as long as possible between loads.
- Identify an off-farm site for the livestock farm delivery and commercial pickup of animals for rendering.
- Keep a record of all deliveries. In the event of a disease being confirmed this may help in identifying the source.
- Ensure that sources of feed and bedding are protected and that samples of delivered feed are "banked" for future analysis in case of an animal disease outbreak.

Keep record of stock movement onto and off the farm

- Participate in the premises and livestock identification program.
- Verify health and origin of purchased livestock.
- New stock entering the herd should be quarantined, observed for 30 days and tested as suggested by your veterinarian prior to entry.
- Keep complete records of all stock movement onto and off of the farm.
- Each farm premises must be treated as a separate unit; record animal movement between units.
- Avoid contact of your farm animals with those of your neighbors.

Keep dogs, cats, birds, wild game and vermin under control

Since other animals and birds can serve as a source of disease entering the herd it is vitally important to make every effort for their elimination or control.

Provide for family and animal health and comfort

The farm should have an emergency 3-day supply of food and drinking water and feed for animals and poultry.

Report any unusual signs of animal sickness or death to your veterinarian.

Disinfection of Premises and Fomites

First, remove organic matter; scrub with soap and water.

Virkon S

- The only disinfectant labeled for foot-and-mouth disease. Works fairly well in organic matter
- Effective against hog cholera virus, many other viruses, bacteria, and fungi.
- Needs 5 – 10 minutes contact time, long activity on hard surfaces
- Comes as a powder, follow directions for 1 percent solution for all uses
- Should be mixed fresh, lasts about five days, color changes when losing potency, test strips included

Bleach/Hypochlorite

- 3 percent dilution, 1/2 cup to 1 gallon water, mix fresh for each use
- Effective against FMD and hog cholera viruses and most other viruses, bacteria, fungi, and spores; requires 10 minutes contact time, inactivated by organic matter
- Inexpensive, Clorox best brand for use

Iodophores and Iodine

- Not effective against foot-and-mouth virus
- Kills most viruses, bacteria, and fungi; inactivated by organic matter
- Requires 10 minutes, contact time
- Questionable efficacy against hog cholera and other swine viruses
- Expensive

Chlorhexidine; Nolvasan

- Questionable effect against FMD virus, not effective against some other bacteria and viruses, not effective against spores
- Requires 10-minute contact time
- Inactivated by organic material

Quaternary Ammonium Compounds

- Roccal D or Roccal
- Not effective against FMD virus; otherwise, kills a wide range of bacteria, viruses, and fungi; does not kill spores
- Requires 10 minutes, contact time
- Works well in organic matter at neutral or high pH
- May be combined with detergents
- Toxic to cats

White Vinegar

- Use 1 gallon per gallon water, works well against FMD virus
- 5-minute contact time

Sodium Carbonate (soda ash, washing soda)

- Strong alkalizing agent
- Effective in dry powder form or as 4 percent solution to disinfect FMD virus-contaminated barns, pens corrals, etc.; caution when applying (surgical mask, coveralls, gloves)

Vesicular Diseases Reference Chart

	Foot & Mouth Disease	Vesicular Stomatitis	Swine Vesicular Disease	Vesicular Exanthema of Swine
Importance	**These 4 diseases are clinically indistiguishable from each other, particularly in swine.**			
Incubation Period	Ingestion 1-3 days, Exposure 3-5 days	Animals 3-5 (up to 21) days, Humans 24-48 hours	Ingestion 2-3 days, Exposure 2-7 days	18-72 hours
Clinical Signs by Species	**All vesicular diseases produce a fever with vesicles that progress to erosions in the mouth, nares, muzzle, teats, and feet**			
Cattle	*Disease Indicators* Oral & hoof lesions; salivation, drooling; lameness; abortions; death in young animals; "panters"	Vesicles in oral cavity, mammary glands, coronary bands, interdigital space	Not affected	Not affected
Pigs	*Amplifying Hosts* Severe hoof lesions; hoof sloughing; snout vesicles; less severe oral lesions	Same as cattle	Severe signs in animals housed on concrete; lameness; salivation; neurological signs; more severe in young	Deeper lesions with formation of granulation tissue on the feet
Sheep & Goats	*Maintenance Hosts* Mild signs if any	Rarely show signs	Not affected	Not affected
Horses, Donkeys, Mules	Not affected	Most severe with oral and coronary band vesicles; drooling; rub mouths on objects; lameness	Not affected	Not affected
Humans	Not common	Flu-like signs, headache, rare oral blisters	Not affected	Seroconversion and mild clinical disease of meningitis in one lab worker
Clinical Summary	Salivation and lameness with vesicles; Equidae not affected	Horses are affected; less contagious so spread is slower; lesions in one area of body	Pigs only; mild lesions; no mortality	Pigs only; deeper lesions; low mortality
Sample Collection	**Before collecting or sending any samples, the proper authorities should be contacted. Samples should only be sent under secure conditions to authorized laboratories to prevent spread.**			
Prefer	Epithelium from unruptured or recently ruptured vesicles in proper medium			
Additional samples/ tissues	Esophageal-pharyngeal fluid (cattle) or throat swab (pigs), 5ml blood with anticoagulant; 10ml for serum, lymph nodes, thyroid, adrenal gland, kidney, heart in formalin	Vesicular fluid collected aseptically and frozen	Vesicular fluid collected aseptically and frozen; unclotted whole blood from febrile animals; fecal and serum samples from infected and noninfected animals	Vesicular fluid collected aseptically and frozen; unclotted whole blood from febrile animals; fecal and serum samples from infected and noninfected animals
Notification	**State & Federal Veterinarians should be contacted IMMEDIATELY and informed of suspicions**			
Quarantine	**State & Federal Veterinarians should be contacted IMMEDIATELY and informed of suspicions**			

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Vesicular Diseases Reference Chart-Additional Information

	Foot & Mouth Disease	Vesicular Stomatitis	Swine Vesicular Disease	Vesicular Exanthema of Swine
Etiology	Aphthovirus	Vesiculovirus	Enterovirus	Calicivirus
Geographic Distribution	Endemic in Asia, Africa, Middle East, parts of S.Amer; US free since 1929	N & Central Amer, northern South Amer	Many European countries	U.S. only (eradicated in 1956)
Transmission	Respiratory aerosols; direct and indirect contact	Insect vectors (sand & black flies); contact, aerosol in humans	Ingestion of contaminated meat; contact with animals, feces	Ingestion of pork contaminated, uncooked garbage
Post-Mortem Lesions	Single or multiple vesicles, ruptured vesicles with demarcation line, "dry" lesions in big oral cavity, coronitis, hoof wall separation, "Tiger heart" lesions, rumen pillar lesions	Similar to FMD, but without heart and rumen lesions	Similar to FMD	Similar to FMD
Differentials	Rinderpest, Bovine Herpes Virus 1 (IBR), BVD, Bovine Papular stomatitis, Malignant Catarrhal Fever, Bluetongue, Contagious Ecthyma, lip and leg ulceration, foot rot, chemical and thermal burns.			
Morbidity & Mortality	Morbidity 100%; Mortality less than 1%, severe in young	Morbidity varies, up to 90%; Mortality low; death in young less common	Morbidity is low; lesions less severe; Mortality not a concern	Morbidity varies, up to 100%; Mortality is low
Sample Packaging	Caution with dry ice as carbon dioxide will inactivate the virus	Virus inactivated by 1% formalin		
Disinfection	2% sodium hydroxide (lye), 4% sodium carbonate, 0.2% citric acid; Resistant to iodophores, quaternary ammonium compounds, hypochlorite and phenol, especially with organic matter present.	2% sodium hydroxide (lye), 4% sodium carbonate, 2% iodophores, chlorine dioxide	10% formalin, 2% sodium hydroxide (lye), iodophores, chlorine dioxide	*Organic matter:* 1% sodium hydroxide combined with detergent *No Organic Matter:* oxidizing agents and iodophores with detergents
Prevention & Control	Destroy litter and susceptible animal products	Control insects, no movement of animals from farm for 30 days		

Exotic Newcastle Disease and Highly Pathogenic Avian Influenza Reference Chart

	Exotic Newcastle Disease (END)	Highly Pathogenic Avian Influenza (HPAI)
Importance	**Highly contagious, often fatal disease**	
Organism	Avian *paramyxovirus-1*	Type A Influenza virus, Orthomyxovirus; Classified by surface antigens H and N
Clinical Signs in Birds	**END and HPAI are clinically indistinguishable from each other** **Respiratory:** Coughing, sneezing, nasal discharge **Digestive:** Watery diarrhea **Nervous:** Depression, ataxia, torticollis Sudden death without clinical signs, decreased egg production, thin-shelled eggs	
Clinical Signs in Humans	Mild conjunctivitis	Mild to fatal disease
Transmission	Spread by feces and respiratory discharges, direct contact, aerosolization and fomites.	
Differential Diagnosis	**Poultry:** HPAI, fowl cholera, infectious coryza, fowl pox, avian chlamydiosis, infectious laryngotracheitis, mycoplasmosis, infectious bronchitis, management problems. **Psittacines:** Avian chlamydiosis, Pacheco's disease, avian influenza, salmonellosis, toxicosis.	END, infectious laryngotracheitis, acute bacterial diseases (eg. fowl cholera and *E. coli* infections)
Morbidity/ Mortality	Mortality can reach 100%; Morbidity can reach 90%	Mortality can reach 100%; Morbidity can reach 100%
Diagnosis	Virus isolation required for definitive diagnosis	
Sample Collection	**Before collecting or sending any samples, the proper authorities should be contacted. Samples should only be sent under secure conditions to authorized laboratories to prevent spread.**	
Prefer	Tracheal or cloacal swabs from live or dead birds, as well as feces.	
Notification	**State & Federal Veterinarians should be contacted IMMEDIATELY and informed of suspicions**	
Quarantine	Suspected animals, areas, farms will be quarantined by the state veterinarian.	
Vaccination	Routine in poultry flocks. Will not prevent infection or virus shedding.	Costly; no cross protection; may result in reassortment viruses. Inactivated H5 vaccine licensed in US for emergency use
Disinfection	Virus killed by extremes of pH, heat, dryness. Phenolics (eg. One Stroke Environ), oxidizing agents (eg. Virkon) and quaternary ammonium compounds (eg. Roccal-D Plus) Halogens (eg. 5% household bleach) Biguanides (eg. Nolvasan-S) Ultraviolet and sunlight	Aldehydes in presence of organic matter Dilute acids (eg. paracetic acid)

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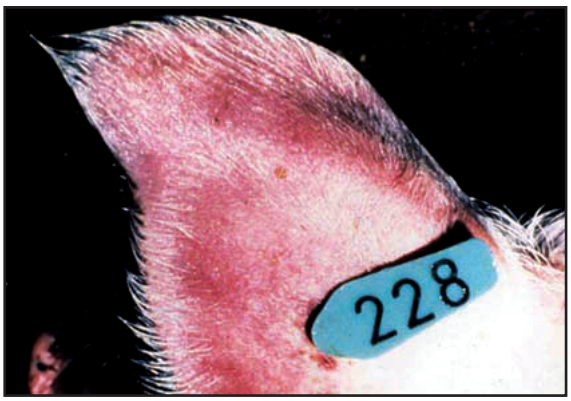
Section 4

Photographs

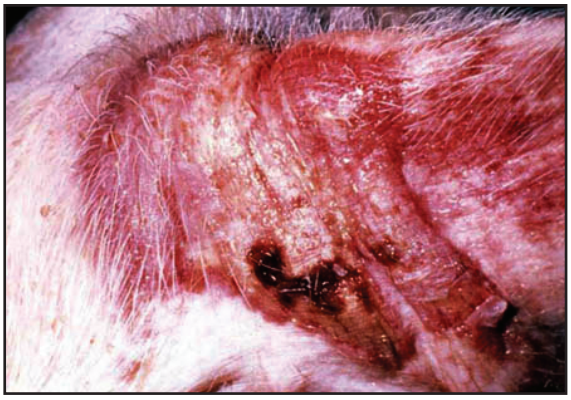
ASF2



African Swine Fever

ASF 2—Pig with African swine fever. Reddened skin on the extremities is a non specific lesion associated with a septicemic/viremic condition.

ASF3



African Swine Fever

ASF3—Pig with African swine fever. Necrosis of the skin is a frequent lesion in chronic ASF.

HPAI1

Avian Influenza, Highly Pathogenic

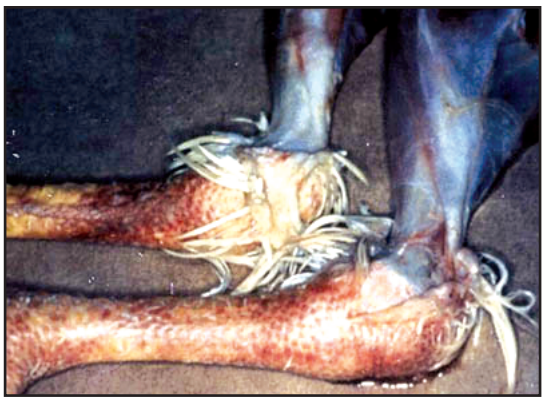
HPAI 1—Edema of the wattles of a chicken with highly pathogenic avian influenza.

HPAI2

Avian Influenza, Highly Pathogenic

HPAI 2—Cyanotic comb of a chicken on the left with highly pathogenic avian influenza compared with a normal chicken on the right.

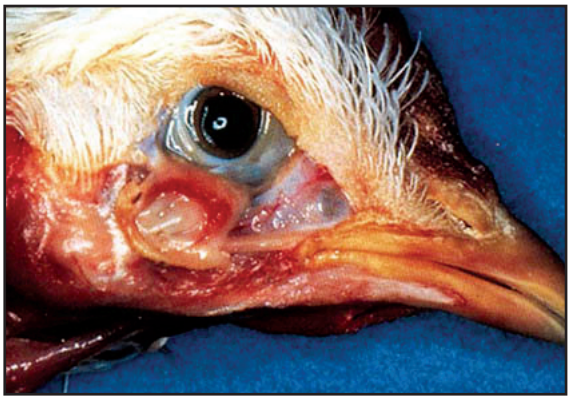
HPAI3



Avian Influenza, Highly Pathogenic

HPAI 3—Congestion and petechiae in the skin on the hocks and shanks of a chicken with highly pathogenic avian influenza.

ND1



Exotic Newcastle Disease

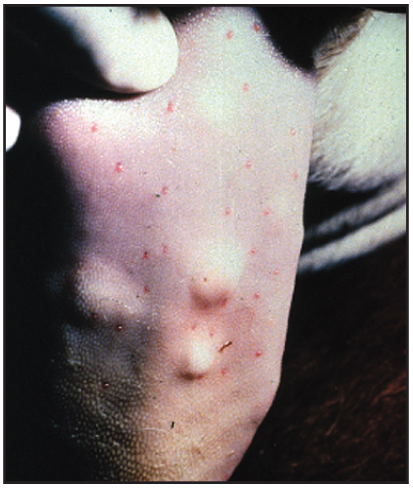
ND 1—Edema and hemorrhage in the reflected lower eyelid of a chicken with exotic Newcastle disease.

FMD1

Foot-and-Mouth Disease, Bovine

FMD 1—Excessive salivation in a cow 24 hours after experimental inoculation with foot-and-mouth disease virus. Note the ring of saliva on the floor.

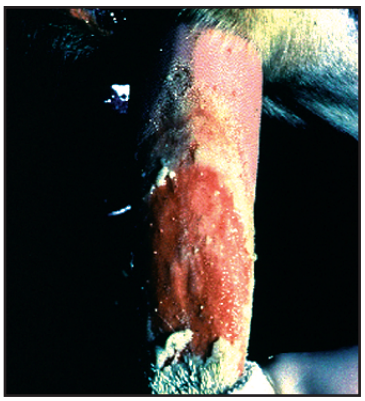
FMD2



Foot-and-Mouth Disease, Bovine

FMD 2—Tongue of the same cow with three small, unruptured vesicles about 36 hours after inoculation.

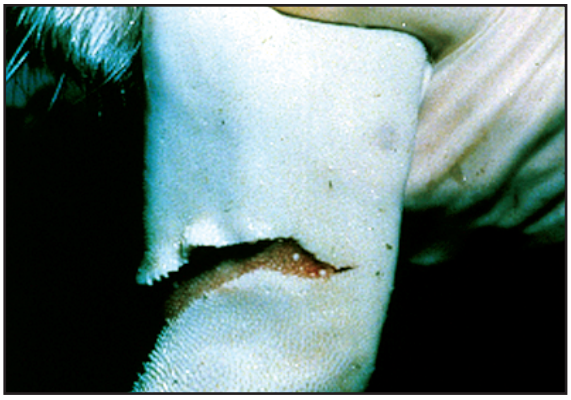
FMD3



Foot-and-Mouth Disease, Bovine

FMD 3—The tongue of the same cow five days after inoculation. Most of the white, blanched epithelium has sloughed off. There are still fragments of white, necrotic epithelium on the surface of the tip of the tongue.

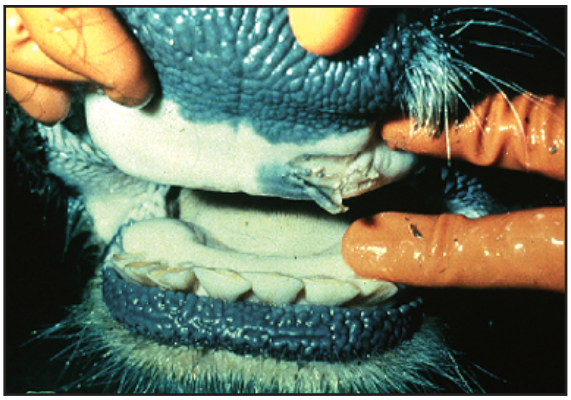
FMD4



Foot-and-Mouth Disease, Bovine

FMD 4—Cow with foot-and-mouth disease. Tongue with a large ruptured vesicle — excellent specimen for diagnosis.

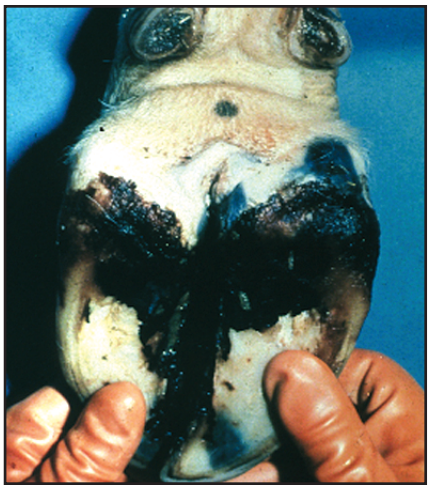
FMD5



Foot-and-Mouth Disease, Bovine

FMD 5—Cow with foot-and-mouth disease. Ruptured vesicle in the gingiva of the dental pad. This sign could be confused with a traumatic injury. The tags of epithelium should be collected for a diagnostic specimen. This lesion is similar to bluetongue in cattle.

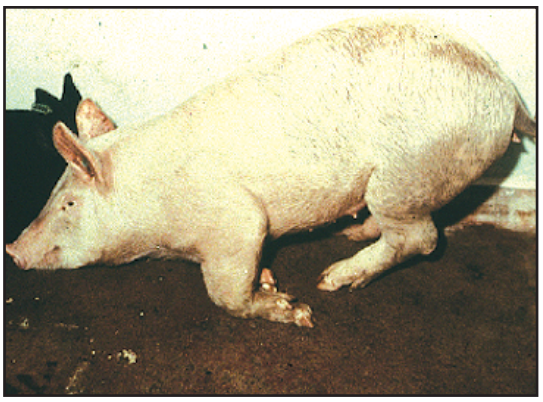
FMD6



Foot-and-Mouth Disease, Bovine

FMD 6—Cow with foot-and-mouth disease. Blanching and vesicles along and above the coronary band of both claws. Note that the vesicles join over the interdigital space.

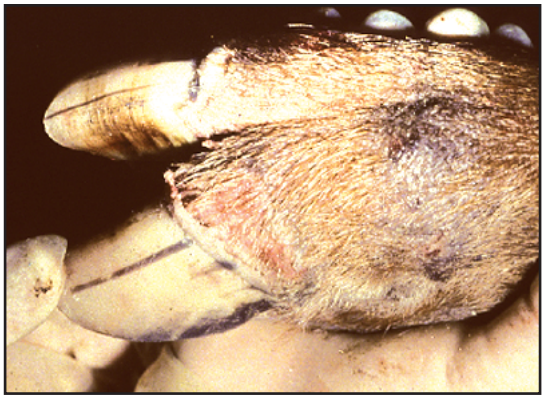
FMD9



Foot-and-Mouth Disease, Swine

FMD 9—In swine the feet are more severely infected from foot-and-mouth disease virus than the nose and tongue. The primary clinical sign in swine is lameness, as shown by walking on the knees.

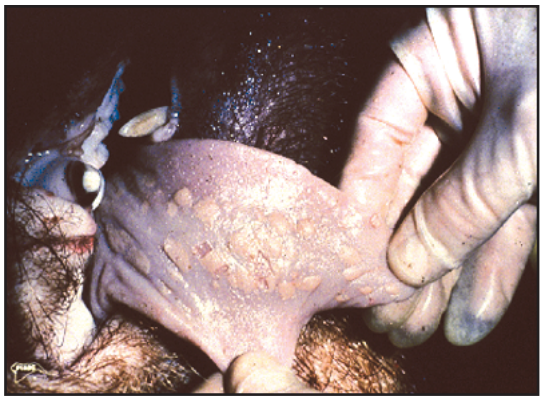
FMD10



Foot-and-Mouth Disease, Swine

FMD 10—Pig with foot-and-mouth disease. The vesicle in the coronary band has ruptured, and the area above the coronary band has eroded.

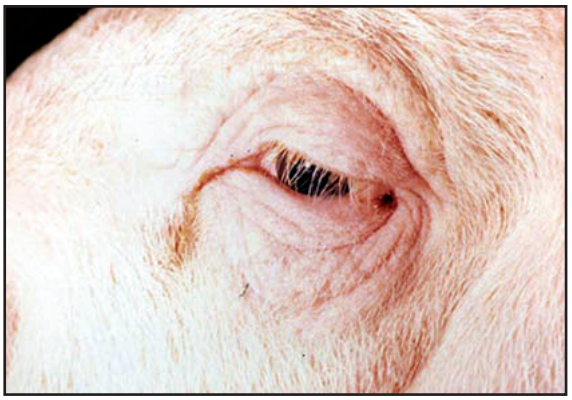
FMD12



Foot-and-Mouth Disease, Swine

FMD 12—Pig with foot-and-mouth disease. The whitish areas on the surface of the tongue are dry FMD lesions. Oral lesions are less frequent in pigs than in cattle, but when they do occur in pigs, the lesions are usually the dry type.

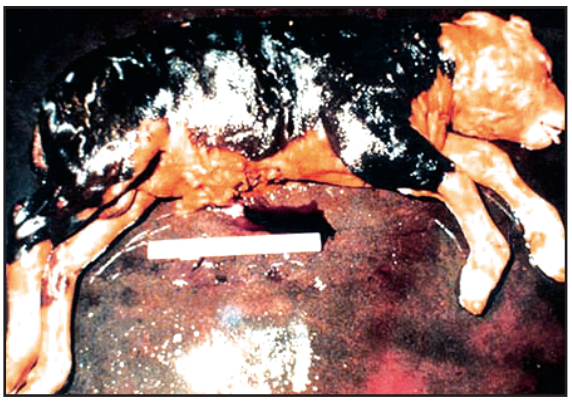
HC1



Hog Cholera/Classical Swine Fever

HC 1—Conjunctivitis and exudate in the medial canthus of a pig infected with hog cholera.

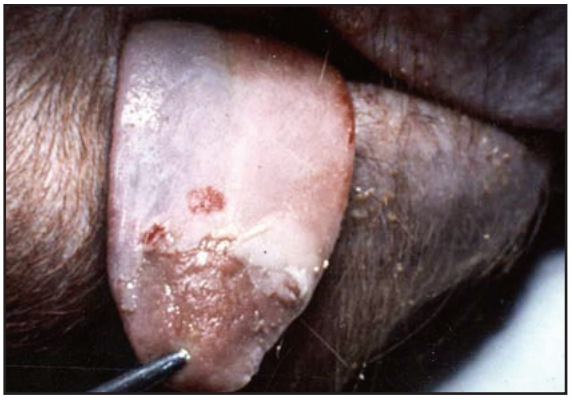
RVF1



Rift Valley Fever

RVF 1—Fetuses can be aborted at any stage of gestation in cattle with Rift Valley fever.

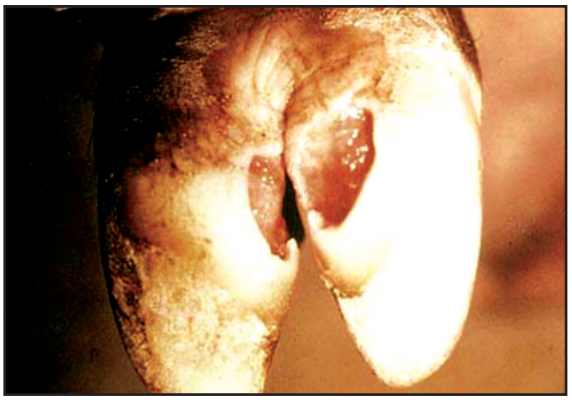
SVD1



Swine Vesicular Disease

SVD 1—Erosions on the tongue of a pig with swine vesicular disease are similar to those resulting from foot-and-mouth disease.

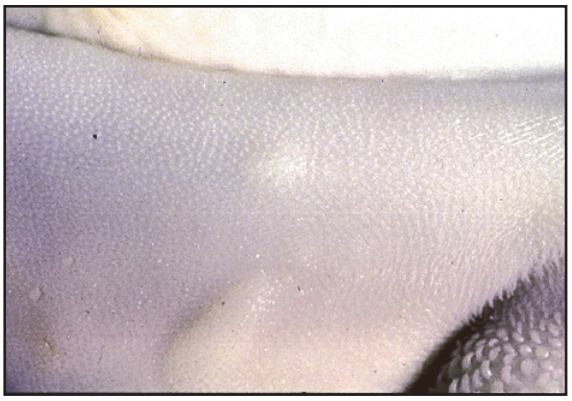
SVD2



Swine Vesicular Disease

SVD 2—Ruptured vesicles on the heel of a pig with swine vesicular disease are indistinguishable from foot-and-mouth disease.

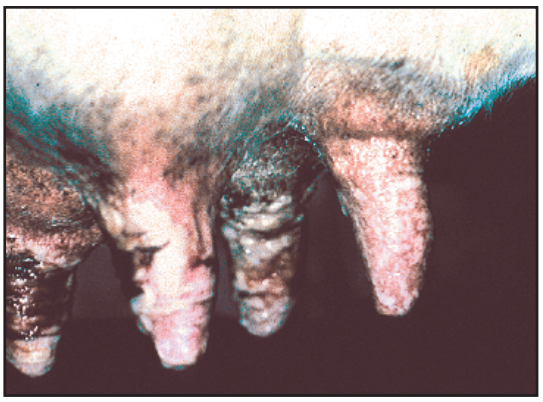
VSBOV2



Vesicular Stomatitis

VS bov 2—Vesicles on the tongue of a cow with vesicular stomatitis.

VSBOV3



Vesicular Stomatitis

VS bov 3—Vesicles and erosions on the teats of a cow with vesicular stomatitis.

VSEQ5

Vesicular Stomatitis

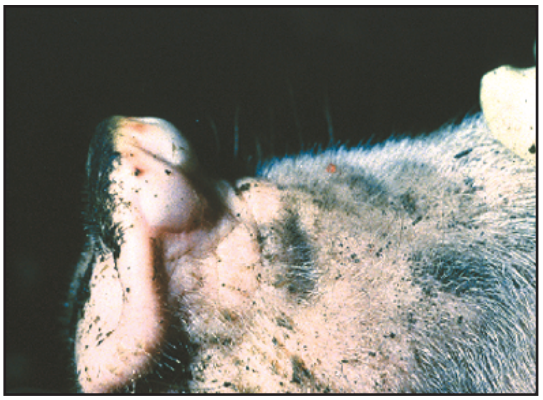
VS eq 5—Erosions and ruptured vesicles on the gingiva of a horse with vesicular stomatitis.

VSEQ7

Vesicular Stomatitis

VS eq 7—Erosions and dried exudate on the coronary band of a horse with vesicular stomatitis.

VSPOR8



Vesicular Stomatitis

VS por 8—A large vesicle on the snout of a pig with vesicular stomatitis.

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Notes